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The Chemistry on Diterpenoids in 1970

Eiichi FUJITA*

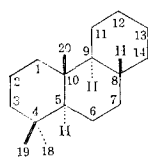
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I. INTRODUCTION

This is one of a series of the annual reviews¹⁻⁶⁾ on diterpenoids chemistry by the author.

In principle, in each section the full papers are first described and the short communications followed. The order of the journals follows the alphabet of their name.

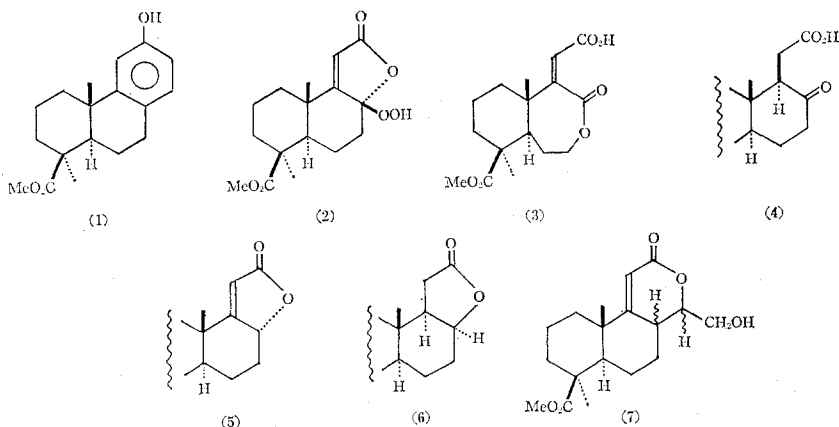
II. PODOCARPANE DERIVATIVES**



Podocarpane

The mass spectrometric studies of podocarpa-8, 11, 13-trien-7-ones were carried out using the labelled derivatives, and it was shown that these compounds underwent essentially the same reactions on electron impact as the corresponding non-oxo compounds.⁷⁾

Low temperature ozonolysis of methyl podocarpate (1) in methanol-methylene chloride resulted in the formation in high yield of hydroperoxy lactone 2. Ozonolysis followed by hydrogen peroxide work-up gave the lactone acid 3, whilst ozonolysis followed by reduction with NaBH₄ gave keto-acid 4 and lactones 5 and 6 derived from peroxide 2 together with δ -lacton 7 possessing all 18 carbon atoms of methyl podocarpate. The lactone 5



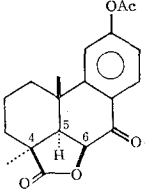
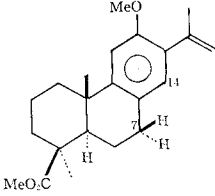
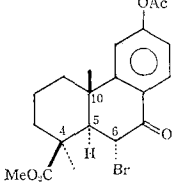
* 藤田 栄一: Laboratory of Physiological Activity, Institute for Chemical Research, Kyoto University, Uji, Kyoto.

** See also section VI, refs. 63, 65, 67, and 70.

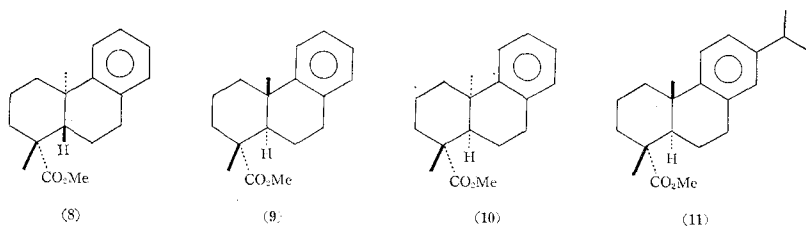
was shown to possess an 8β -H-configuration by application of the nuclear Overhauser effect.⁸⁾

A linear relationship between the intramolecular nuclear Overhauser effect (n. O. e.) and the sixth power of the internuclear distance for protons in reasonably compact organic molecules in deuterio-chloroform solution was derived. It was shown that application of the observed n. O. e. between two protons or between a proton and a methyl group can be used to determine internuclear distances in unknown structures.⁹⁾ (see Table 1)

Table 1.

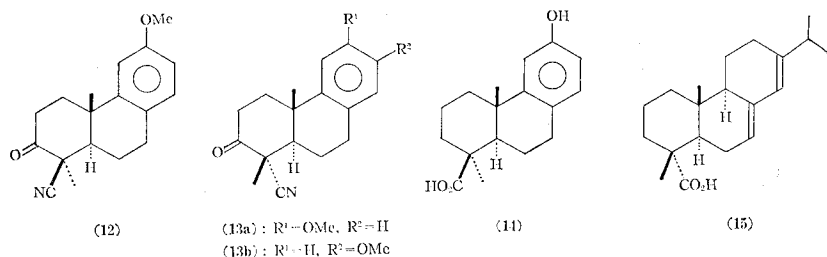
Structures	Proton irradiated	Proton observed	n. O. e (%)	Internuclear distance (Å)
	C- 5-H	C- 6-H	22	2.50
	C- 4-Me	C- 5-H	20	2.80
	C- 4-Me	C- 6-H	14	3.02
	C- 7-H(eq.)	C-14-H	18	2.58
	C- 7-H(ax.)	C-14-H	12	2.97
	C- 4-Me	C- 6-H	22	2.76
	C-10-Me	C- 6-H	10	3.25

Temperature dependent proton magnetic resonance studies of four basic ring C aromatic tricyclic diterpenes (8~11) were carried out, and the characterization of each stereoisomers was shown to be possible. This method was also applied to the analyses of 7-oxo- and 20-nor derivatives.¹⁰⁾



Epimeric α -cyano- α -methyl ketones (12 and 13) were prepared by stereoselective reaction of enolates. They were used in syntheses of podocarpic acid (14) and abietic acid (15). Alkylations of β -ketonitriles were found to be stereochemi-

Chemistry on Diterpenoids in 1970



cally opposed to those of corresponding β -keto esters. (Chart 1). Syntheses of α -cyano enones by opening of epoxy ketones with cyanide and syntheses of α -cyano ketones by two reductions of α -cyano enones or by trapping of enolates, obtained in Birch reductions of enones, with cyanogen chloride were also reported.¹¹⁾ (Chart 2)

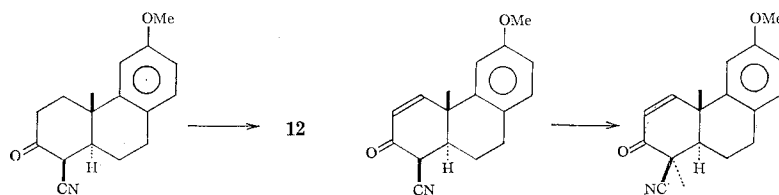


Chart 1

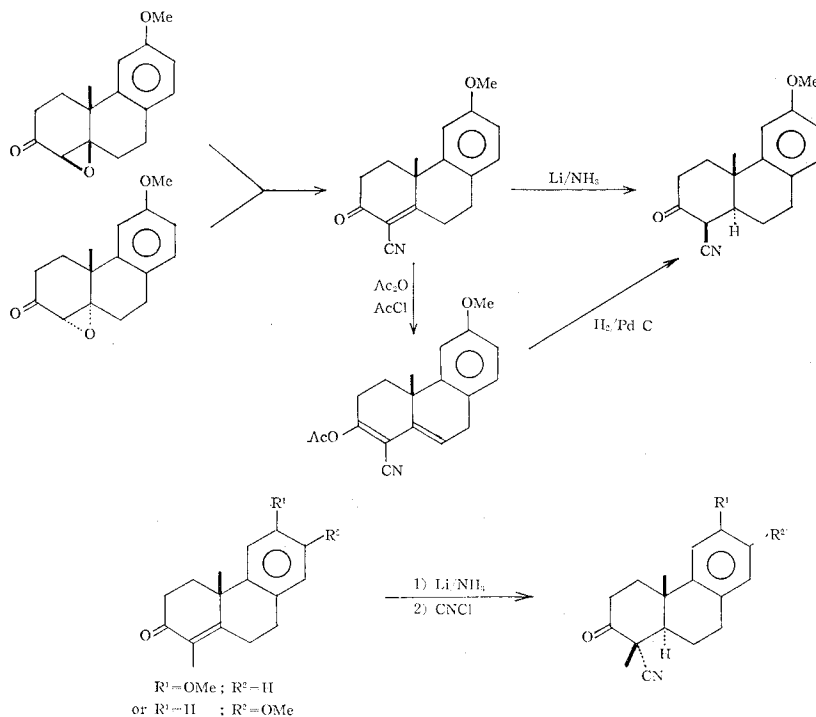
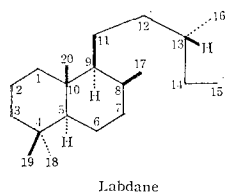


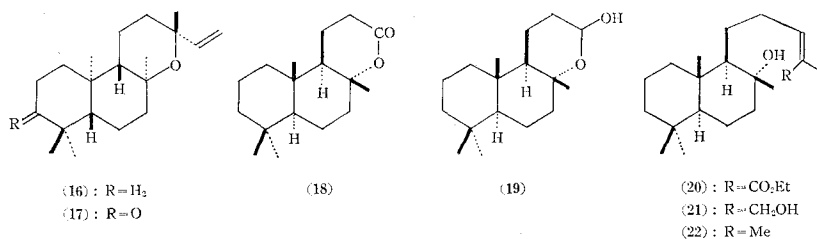
Chart 2

III. LABDANE DERIVATIVES*

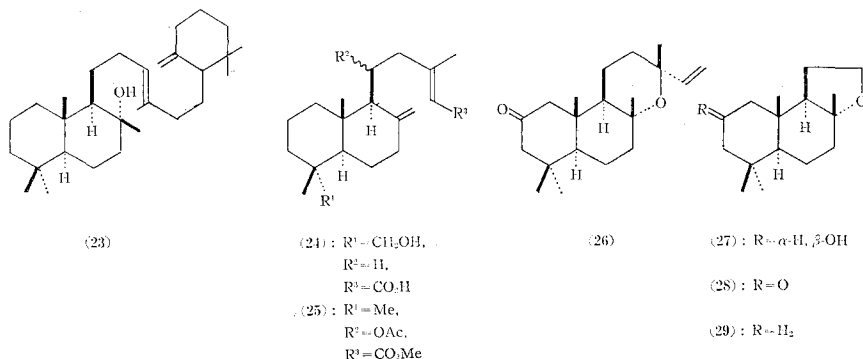


From the ethyl acetate extract of the roots of *Solidago missouriensis*, *ent*-13-epimanoyl oxide (16) and *ent*-3-oxo-13-epimanoyl oxide (17) were isolated,¹²⁾ accompanied by abietane derivatives.**

The condensation of ambreinolal (19), prepared by $\text{LiAl}(\text{OEt})_2\text{H}_2$ reduction of ambreinolide (18), with 2-carbethoxyethylidenetriphenylphosphorane gave the α -methyl-



cis- α , β -unsaturated ester 20, which was converted into the allyl alcohol 21 by reduction with LiAlH_4 . The reaction of hemiacetal (19) with isopropylidenetriphenylphosphorane afforded an isopropenyl derivative 22 with the same olefinic methyl group as that of ambrein (23). By assignment of the NMR spectra of the above compounds structurally related to ambrein (23), it was confirmed that the configuration of ambrein is the *trans* form.¹³⁾

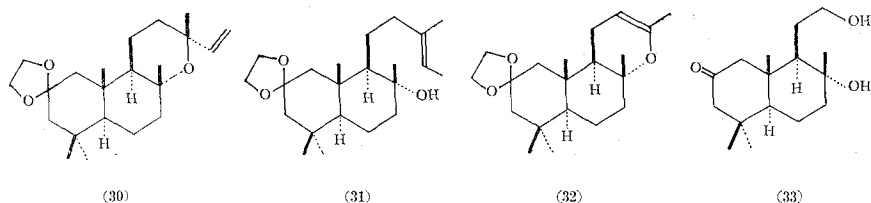


Copaiferolic acid (24) and methyl 11-acetoxylabda-8(17), 13-dien-15-oate (25) were obtained from the oleoresin of *Copaifera multijuga*.¹⁴⁾

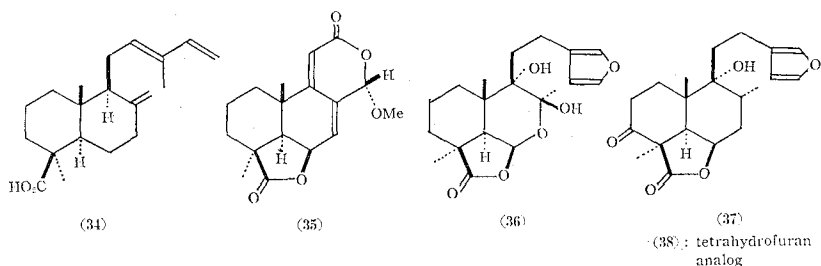
2-Oxomanoyl oxide (26) was converted into the 2-hydroxy ether 27 and the 2-oxo ether 28, both of which had ambergris-type odors similar to but much weaker than that of odoriferous compound 29. The route affording the highest overall yield was *via* the intermediates 30, 31, 32, and 33, which gave 23% of 28 and 17% of 27.¹⁵⁾

* See also section IV, ref. 35.

** See also section VI.



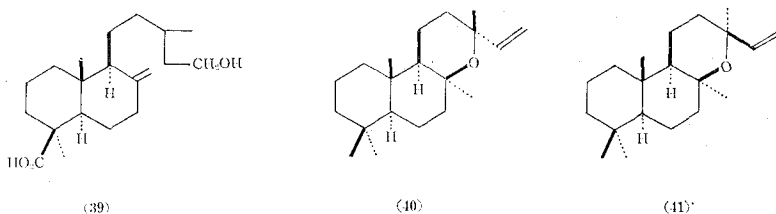
Dundathic acid which had been isolated and named by Baker and Smith¹⁶⁾ was shown to be a polymer consisting principally of units derived from *trans* communic acid (34) by Carman *et al.*¹⁷⁾



The structure of a novel $C_{17}H_{20}O_3$ terpenoid antifungal agent, LL-Z 1271 α , which was isolated from fermentations of an unidentified *Acrostalagmus* species, was elucidated to be 35 by a research group of American Cyanamid Company.¹⁸⁾ In addition, the chemistry of some interesting base hydrolysis products of this mold metabolite was discussed. Biogenetically, it could arise from microbiological degradation of a normal diterpene of the labdane type by oxidative cleavage between C-12 and C-13. A reasonable alternative would be the addition of a C_1 unit to C-11 of a sesquiterpene precursor of the drimenin class.

A new diterpenoid isolated from *Leonotis dysophylla* was shown to be 8-hydroxymarrubiin (36). The 8-hydroxy group is probably β -oriented.¹⁹⁾

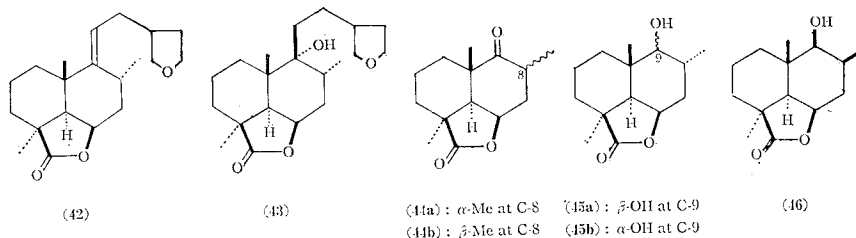
The structure and stereochemistry of peregrinin and tetrahydroperegrinin, which were isolated together from *Marrubium peregrinum*, were established to be 37 and 38.²⁰⁾ Imbricatolic acid (39) was isolated from the resin of *Cupressus nevadensis* and shown to be present in the resins of several American and Asian *Cupressus* species but absent from that of the European species *C. sempervirens*.²¹⁾



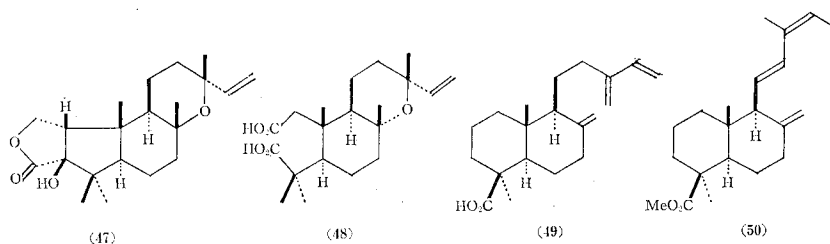
Analysis of the volatile leaf oil of *Chamaecyparis nootkatensis* showed some monoterpenes as the main constituents and the presence of nine diterpene hydrocarbons (unknown diterpene I, isopimara-8(9),15-diene, isohibaene, sandaracopimaradiene, isophyllocladene, isopimaradiene, phyllocladene, abieta-7,13-diene, and dehydroabietadiene) and the following diterpenes: 13-epimanoyl oxide, 8-

epimanoyl oxide (40), 8,13-diepimanoyl oxide (41), and phyllocladan-16-ol.^{22a, b)}

Anhydrotetrahydromarrubiin (42) was reconverted into tetrahydromarrubiin (43). Ozonolysis of 42 to the trimethyl keto lactone 44a did not involve change of the C-8 configuration. Reduction of 44a with borohydride gave the trimethyl-hydroxy lactones 45a and 45b; the epimeric keto lactone 44b was reduced to 46.²³⁾



A homo-diterpene lactone isolated from *Dacrydium colensoi* was shown to have structure 47.²⁴⁾ The dihydro derivative of 47 was synthesized²⁵⁾ by two inde-

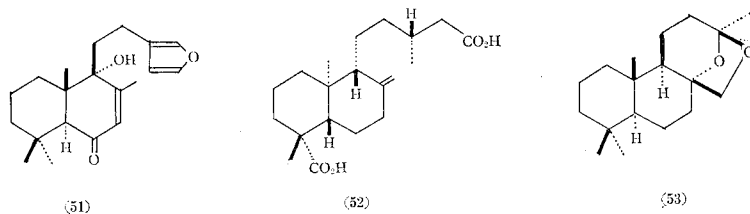


pendent routes, that is, the one from 48 isolated from the heartwood of *D. colensoi* and the other from 2-oxomanoyl oxide (26).

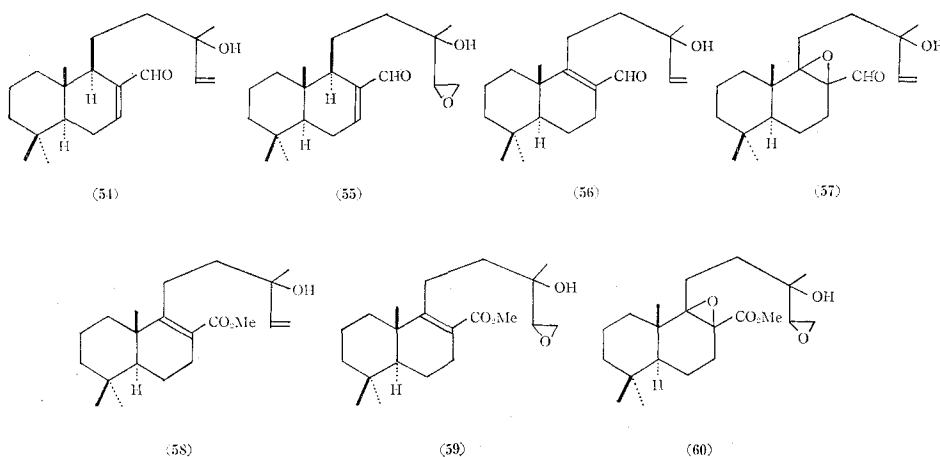
A new diterpene acid, isolated as its methyl ester from *Callitris columellaris*, was shown to be an isomer of *trans*-communic acid (34) and to be represented as 49. Another new isomer of communic acid was shown to result from thermal rearrangement of *trans*-communic acid methyl ester on gas chromatography, and was tentatively assigned the structure methyl labda-8(17)-*trans*-11(12)-*cis*-13(14)-trien-19-oate (50) on the basis of spectroscopic and mechanistic considerations.²⁶⁾

Some reactions—reductions and rearrangements—of solidagenone, the major diterpenoid from *Solidago canadensis* were investigated,²⁷⁾ which substantiated the structure and stereochemistry (51) previously deduced for it. The structure and stereochemistry of oliveric acid, a principal constituent of the trunk resin of *Daniellia oliveri*, were established as 52.²⁸⁾

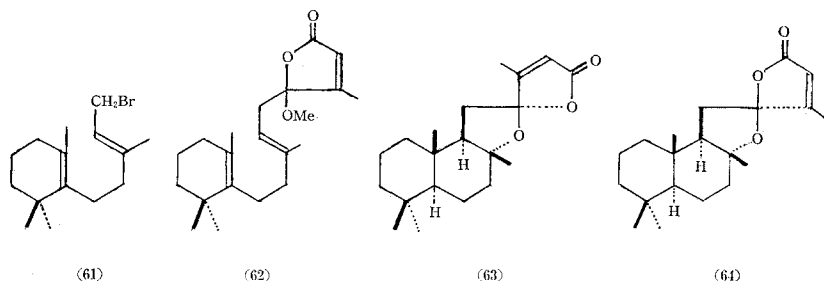
By-products formed during oxidation of sclareol to a lactone were investigated. As the unsaponifiable neutral products, 13-epimanoyl oxide and a smaller



amounts of manoyl oxide and **53** were afforded.²⁹⁾ Selective epoxidation in a series of labdadienes was investigated. Epoxidation of 13-hydroxy-7,14-labdadien-17-al (**54**) with monopero-phthalic acid gave 13-hydroxy-14(15)-epoxy-7-labden-17-al (**55**). However, epoxidation of 13-hydroxy-8,14-labdadien-17-al (**56**) gave 13-hydroxy-8(9)-epoxy-14-labden-17-al (**57**). Oxidation of **56** with silver oxide followed by methylation with diazomethane gave 17-carbomethoxy-8,14-labdadien-13-ol (**58**). Epoxidation of **58** gave a mixture of the 14(15)-epoxy- (**59**) and 8(9),14(15)-diepoxy- (**60**) derivatives of **58**. Selective epoxidation of the labdadiene vinyl group was possible only when the double bond at position 7 was substituted (at C-8) with formyl or carbomethoxy group.³⁰⁾



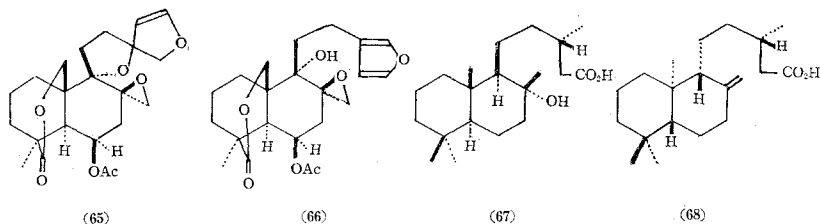
A C_{20} -butenolide **62** was derived from a reaction of monocyclofarnesyl bromide (**61**) with di-3-methylfurylmercury followed by photo-oxidation. A successive treatment of **62** with stannic chloride yielded α - and β -levantenolides (**63** and **64**).^{31a)} A modified route involving one step cyclization of rings, A, B, and C was also published.^{31b)}



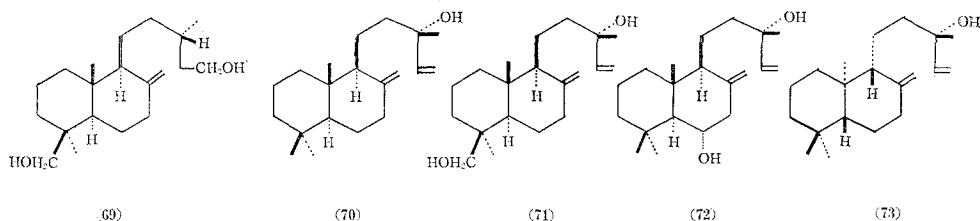
The structure of nepetaefolin, a prefuranoid diterpene isolated from the leaves and stems of *Leonotis nepetaefolia*, was clarified as shown in **65**. The biogenetic implication that **65** is the immediate precursor of **66** in *L. nepetaefolia* was upheld by isolation studies. Details of the biosynthetic processes leading from the isoprenoid skeleton to the spirodihydrofuran system, however, are as yet obscure.³²⁾

About the absolute configurations of several labdane derivatives at C-13, con-

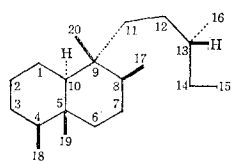
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firmation was presented as follows: labdanolic acid (67), eperuic acid (68), imbricatadiol (69), 13-epimanool (70), 13-epitorulosol (71), larixol (72), and *ent*-13-epimanool (73).³³⁾

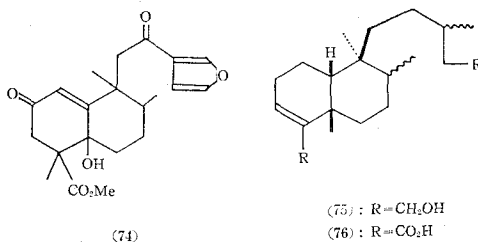


IV. CLERODANE DERIVATIVES



Clerodane

“Chettaphangkhi” is an indigenous drug applied as stomachics in Thailand and is obtained from the roots of *Adenochlaena siamensis*. Several furanoditerpenoids were isolated from the ethylene chloride extract. The structure of chettaphanin-I, the most abundant component, was investigated and the planar structural formula 74 was presented for it.³⁴⁾

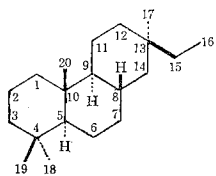


From the neutral saponified products of the petroleum ether extract of *Cistus monspeliensis*, 8 α ,15-labdanediol which has been isolated from *C. labdaniferus* was isolated as a minor component. To the main constituent, cistodiol, structure 75 was assigned. The corresponding diacid, cistodioic acid (76), was also isolated and characterized.³⁵⁾

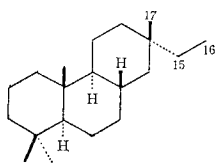
V. PIMARANE AND ISOPIMARANE DERIVATIVES*

The crystal structure of rimuene was determined using three-dimensional

* See also section III, ref. 22.



Pimarane

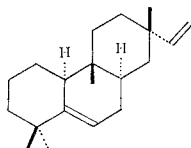


Isopimarane

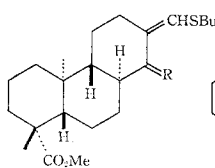
photographic data. The molecular structure was confirmed as 77 in agreement with other studies.³⁶⁾

Total syntheses of racemic 4-epipimaric acid (82a) and 4-episandaracopimaric acid (83a) were done.

The previously described keto ester 78 was transformed, *via* alcohol 79, aldo ester 80, and C-13 epimeric β , γ -unsaturated aldehydes 81, into a mixture of methyl *rac*-4-epipimarate (as 82b) and methyl *rac*-4-episandaracopimarate (as 83b). This was chromatographed on alumina impregnated with silver nitrate to effect separation of the C-13 epimers. The corresponding racemic acids (82a and 83a) were prepared from esters by treatment with potassium *t*-butoxide in DMSO.³⁷⁾

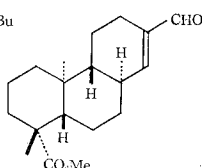


(77)

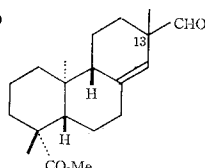


(78) : R=O

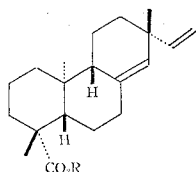
(79) : R=



(80)

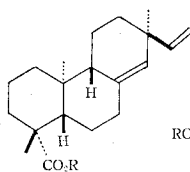


(81)



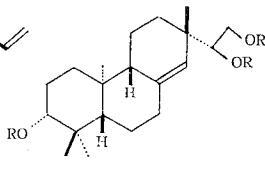
(82a) : R=H

(82b) : R=Me



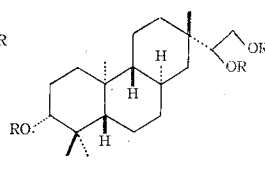
(83a) : R=H

(83b) : R=Me



(84) : R=H

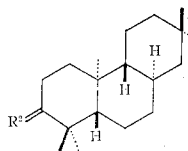
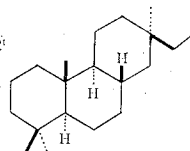
(86) : R=Ac



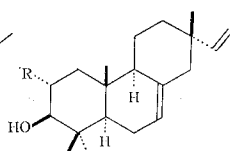
(85) : R=H

(87) : R=Ac

Dihydrodarutigenol (85) was prepared by the hydrogenation of 84 over platinum dioxide at the atmospheric pressure and under 90 kg H. Acetate 86 was reduced under both conditions to give 87.³⁸⁾ Dihydrodarutigenol (85) with meta periodic acid gave aldehyde 88, which was converted by methyl magnesium

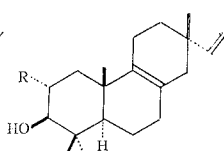
(88) : R¹=CHO,R²= α -OH, β -H(89) : R¹=CH-Me,R²= α -OH, β -H(90) : R¹=Et,R²=H₂

(91)



(92) : R=OH

(93) : R=H



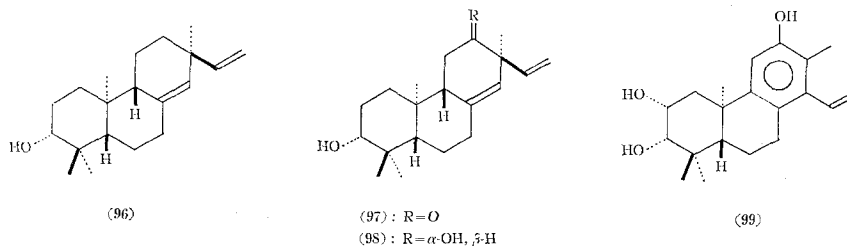
(94) : R=OH

(95) : R=H

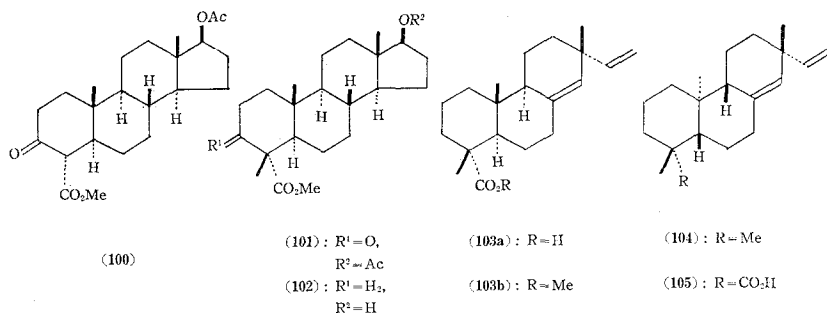
iodide into 89. The compound 89 was transformed by oxidation with chromic anhydride in acetic acid followed by Wolff-Kishner reduction into the hydrocarbon 90, an enantiomer of 91 prepared from dihydropimaric acid.³⁹⁾

Structure of virescenols A and B, metabolites of *Oospora virescens*, was investigated. Virescenol A(92) was prepared by treatment of virescenoside A with hydrochloric acid at 37° for 15 days. Similarly, virescenoside B gave virescenol B(93). Isovirescenol A(94) was obtained by the hydrochloric acid isomerization of virescenol A. Isovirescenol B(95) was prepared similarly.⁴⁰⁾

Three pimarane diterpenes isolated from the heartwood of *Cleistanthus schlechteri* var. *Schlechteri* were identified as *ent*-isopimara-8(14), 15-dien-3 β -ol (96), *ent*-3 β -hydroxyisopimara-8(14), 15-dien-12-one (97), and *ent*-isopimara-8(14), 15-dien-3 β , 12 β -diol (98).⁴¹⁾ These three diterpenes are congeners of the aromatic diterpene cleistanthol (99).



Novel steroidal β -keto ester 100 was prepared by the reductive carbomethoxylation of testosterone acetate. Methylation of 100 afforded selectively 101, whose 3-deoxo ester 102 was converted by a series of reactions into sandaracopimaric acid (103a).⁴²⁾

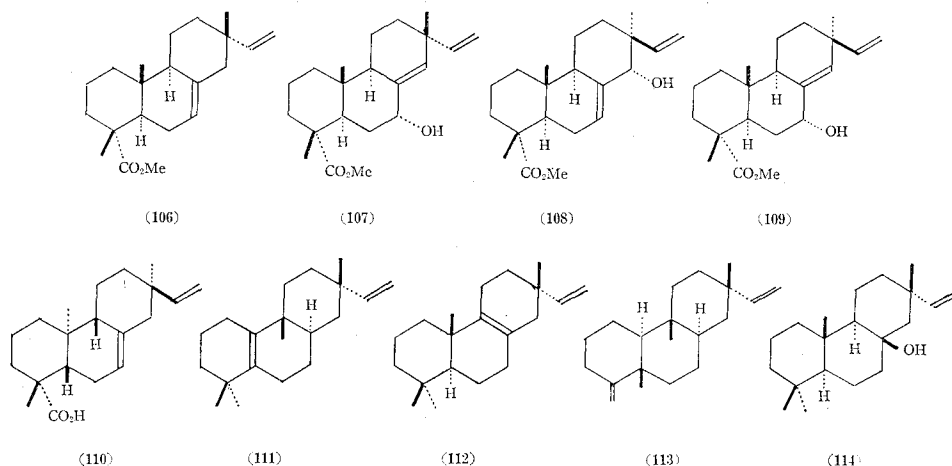


The occurrence of *ent*-pimara-8(14), 15-diene (104), *ent*-pimara-8(14), 15-dien-19-oic acid (105), and *ent*-16-kaurene in *Aralia racemosa* was reported.⁴³⁾

Allylic photosensitized oxidation of methyl isopimarate (106) afforded methyl 7 α -hydroxysandaracopimarate (107) and the same reaction of methyl pimarate gave the hydroxy-ester 108 accompanied by methyl 7 α -hydroxy pimarate (109).⁴⁴⁾

Chemical and spectral studies of the major diterpene acid component of the bark of *Croton oblongifolius* and its conversion products showed that it should be formulated as *ent*-isopimara-7, 15-dien-19-oic acid (110).⁴⁵⁾

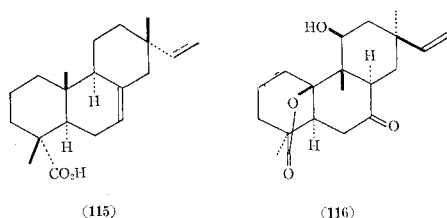
The bp₂ 145~170° fraction of essential oil of *Thuja standishii* was shown to



contain the following diterpenes: $\Delta^{5(10)}$ -rimuene (**111**) (1%), rimuene (77) (9%), $\Delta^{8(9)}$ -sandaracopimaradiene (**112**) (0.5%), hibaene (8%), dolabradiene (**113**) (3%), dehydroabietane (5%), totarol (3%), and 8 β -hydroxyisopimar-15-ene (**114**) (50%).⁴⁶⁾

The calculation of NMR chemical shift values by the method previously published by ApSimon *et al.*⁴⁷⁾ was extended to a derivation of the shielding effect of the ketonic carbonyl group, and applied to a variety of substances, including a selection of diterpenes and their ketonic derivatives.⁴⁸⁾

7-Isopimaren-18-oic acid (**115**) was synthesized from methyl 8(14),15-isopimaradien-18-oate (methyl sandaracopimarate) (**103b**) based on the reactivity of α -epoxides in this series.⁴⁹⁾



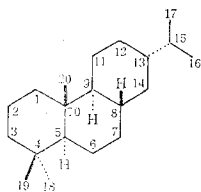
The structure **116** (11 β -hydroxy-rosenonolactone) of rosein III, a metabolite of *Trichothecium roseum*, indicated by chemical and spectroscopic evidence, was confirmed by an x-ray analysis of the metabolite itself, using direct methods of phase determination.⁵⁰⁾

VI. ABIETANE DERIVATIVES*

From the roots of *Solidago missouriensis*, 7,13-abietadien-3-one, -3 β -ol, and -2 α -ol were isolated.^{12)**}

* See also section III, refs. 12 and 22 and section V, ref. 46.

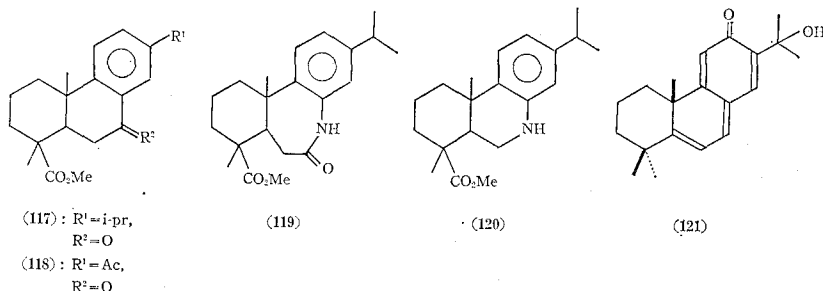
** These abietadienes were found to be *ent*-abietane derivatives and artefacts from corresponding 8(14)-en-13-ols. (Private communication from Dr. Anthonsen to the author.)



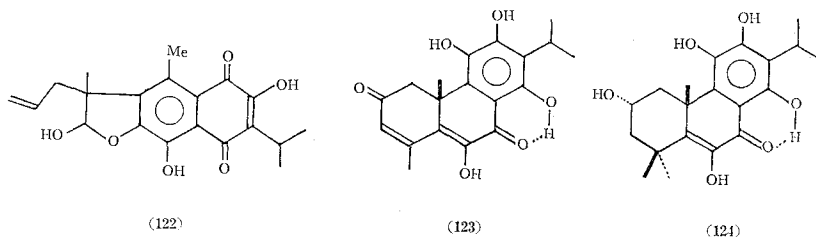
Abietane

structure 120.⁵¹⁾

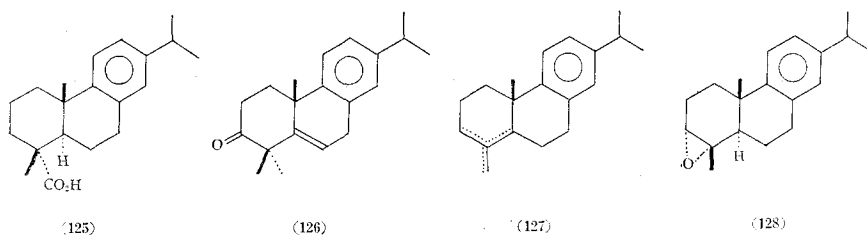
Controlled oxidation of methyl dehydroabietate with chromic anhydride gave methyl 7-ketodehydroabietate (117). Prolonged oxidation yielded increasing amounts of the diketone 118. When subjected to Beckmann rearrangement (polyphosphoric acid) the oxime of the ketone 117 furnished the expected lactam 119. In addition, a weak base was formed, the spectral data of which indicated



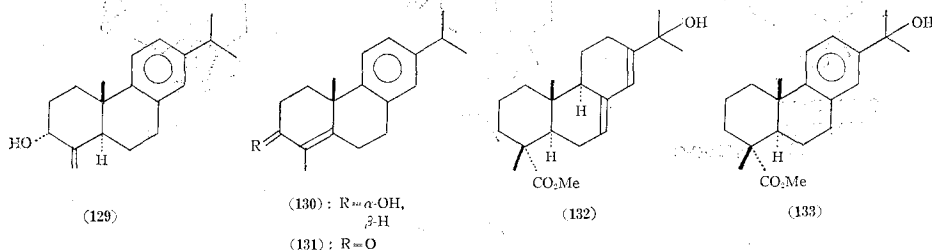
In a review of the recent studies on the plant pigment, Eugster⁵²⁾ described on the diterpene pigments: fuerstion (121) from *Fuerstia africana*, coleon A(122) and coleon B(123) from *Coleus igniarius*, and coleon C(124) from *Coleus aquaticus*.



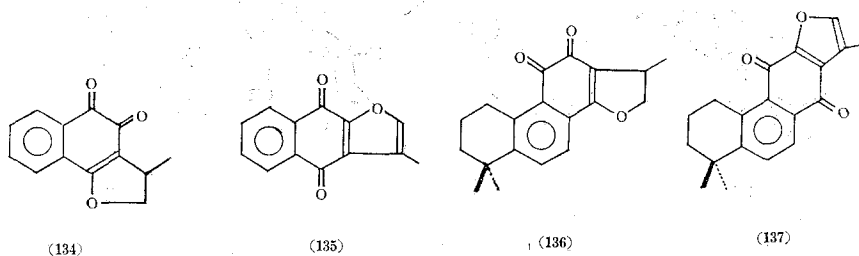
A convenient route from abieta-8,11,13-trien-18-oic acid (125) to abieta-5,8,11,13-tetraen-3-one (126) was developed involving selective epoxidation of the alkene mixture (127) obtained by oxidative decarboxylation of the acid with lead tetraacetate. Treatment of the 3 α ,4 α -epoxide 128 with lithium diethylamide gave a quantitative yield of the allylic alcohol 129. Brief treatment of this alcohol with N-lithioethylenediamine gave the α,β -unsaturated alcohol 130, which on oxidation afforded the enone 131. Methylation of the latter compound with methyl iodide and potassium *t*-butoxide in *t*-butanol yielded 126 in 43% overall yield from the alkene mixture 127. Other reactions of 128 were also reported and discussed.⁵³⁾



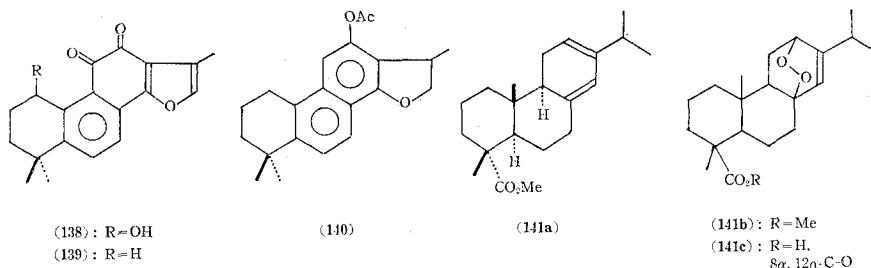
A phytochemical survey of the diterpenoid resin acids of the North Queensland species of *Agathis* was presented. The methyl esters, 132 and 133, of two new resin acids were described.⁵⁴⁾



Compounds, 134 and 135, were synthesized, in relation to cryptotanshinone (136) and isotanshinone-II (137).⁵⁵⁾



Hydrogenolysis under hydrogens over Pd-C in the presence of acid of hydroxytanshinone (138) and tanshinone-II (139) into 140 was investigated, and its mechanism was presented.⁵⁶⁾

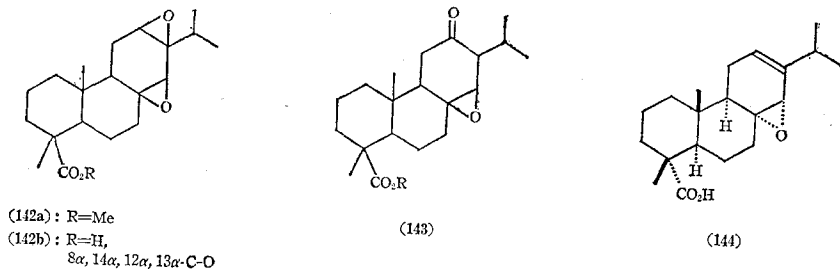


It was shown that the direct irradiation of cyclic peroxides such as ascaridol, and those (*e.g.* 141b) derived from cyclohexadiene, 1,3,5,5-tetramethylcyclohexadiene, and methyl levopimarate (141a) rearranged on irradiation. The bisepoxides (*e.g.* 142a) were obtained as in the thermal rearrangement, together with, where the structure permitted, the keto-epoxide (*e.g.* 143). The mechanism of the reaction was presented.⁵⁷⁾

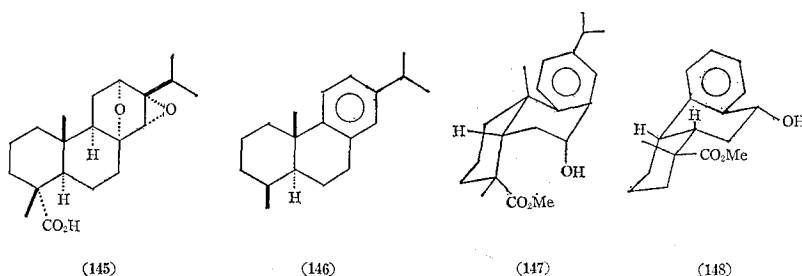
The reaction of levopimaric acid transannular peroxide (141c) with triphenyl phosphine afforded a monoxide whose structure was shown to be 8 α , 14 α -epoxy-abiet-12-en-18-oic acid (144). Since epoxidation of 144 afforded levopimaric acid dioxide, the structure of the latter was shown to be 8 α , 14 α :12 α , 13 α -bisepoxy-abietan-18-oic acid (142b),⁵⁸⁾ which denied the previously proposed structure 145*.

* See ref. 3.

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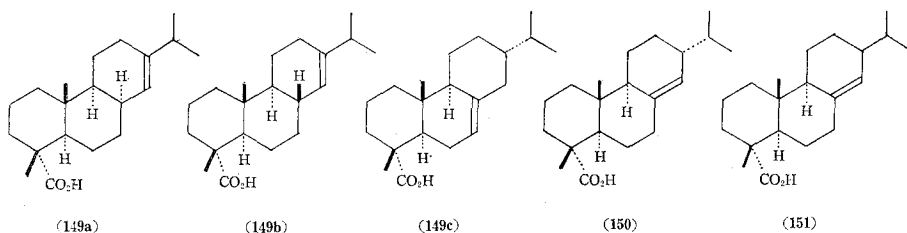


Isolation of 18-norabieta-8, 11, 13-triene (146) from *Thujopsis dolabrata* and from *Podocarpus ferrugineus* was reported.⁵⁹⁾



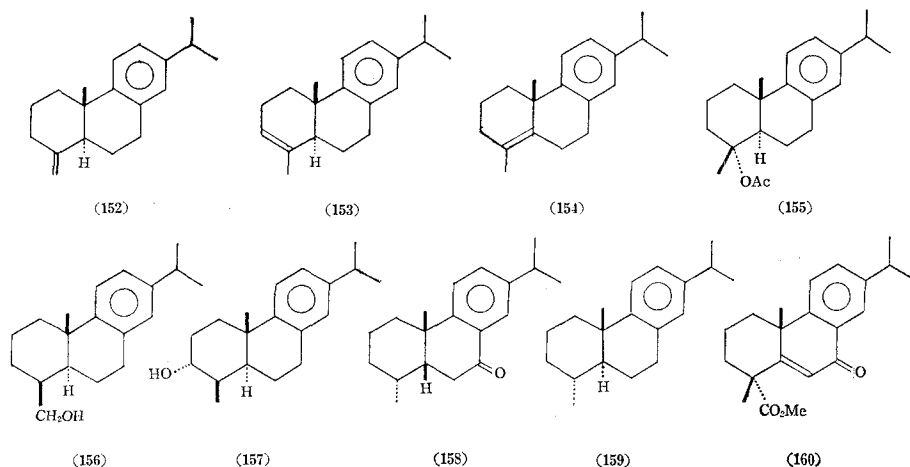
Syntheses of 20-nor tricyclic diterpene derivatives and their structure determinations were reported. In the A/B-*cis* ring system, it was revealed by the analysis of NMR and IR spectra and reactions that the steroid type conformation (147) of C-10 methyl series was preferred to nonsteroid type conformation, conversely, non steroid type conformation (148) was preferred in 20-nor derivatives.⁶⁰⁾

Syntheses of 8 α -abiet-13-en-18-oic acid (149a), abiet-13-en-18-oic acid (149b), and abiet-7-en-18-oic acid (149c) were published. The stereochemical course of various reactions of these compounds as well as those of two abiet-8(14)-en-18-oic acids, 150 and 151, were discussed.⁶¹⁾



It was found that dehydroabietic acid on lead tetraacetate decarboxylation gave three olefins, 152, 153, and 154, and 18-norabieta-8, 11, 13-trien-4-ol acetate (155). Hydroboration-oxidation of the mixture of these olefins gave 18-norabieta-8, 11, 13-trien-19-ol (156) and 18-norabieta-8, 11, 13-trien-3 α -ol (157) as major products and 19-nor-5 β -abiet-8, 11, 13-trien-7-one (158) as a minor product. The reduction of dehydroabietonitrile with sodium in liquid ammonia gave 19-nor hydrocarbon 159, instead of 18-norabieta-8, 11, 13-triene suggested first. The

structure of 158 was confirmed by a two-steps synthesis from methyl 7-oxoabieta-5,8,11,13-tetraen-18-oate **160**: a vigorous basic hydrolysis accompanied by decarboxylation and hydrogenation over rhodium catalyst.⁶²⁾



Synthesis of (+)-4-epidehydroabietic acid (**161**) from podocarpic acid was accomplished as shown in Chart 3, which constituted a formal total synthesis of **161**.⁶³⁾

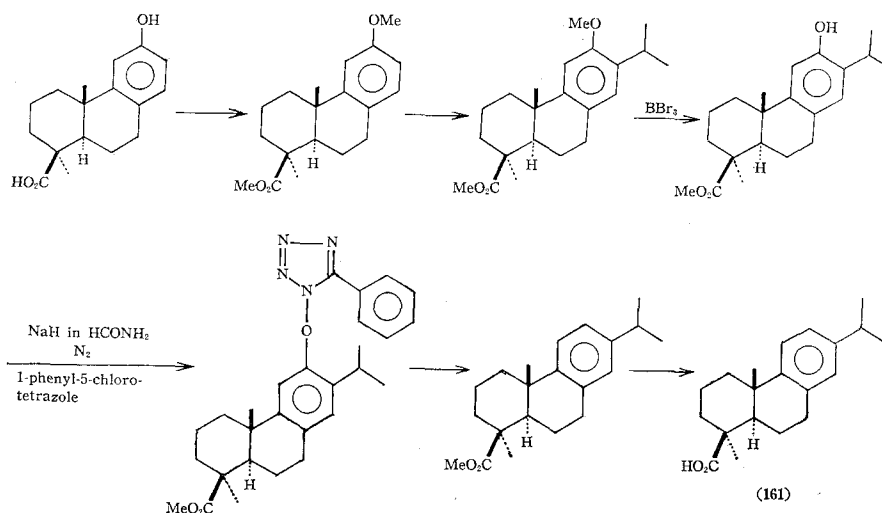
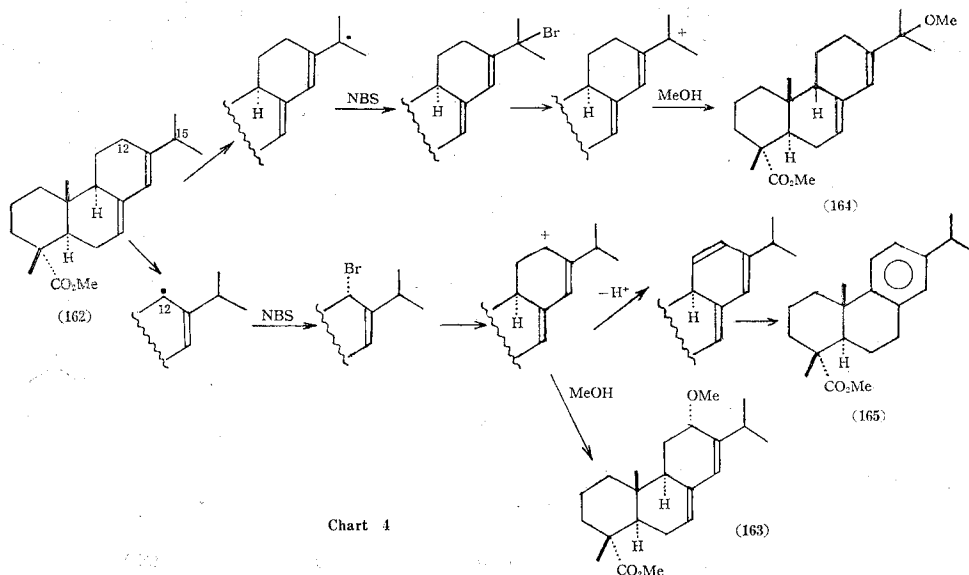
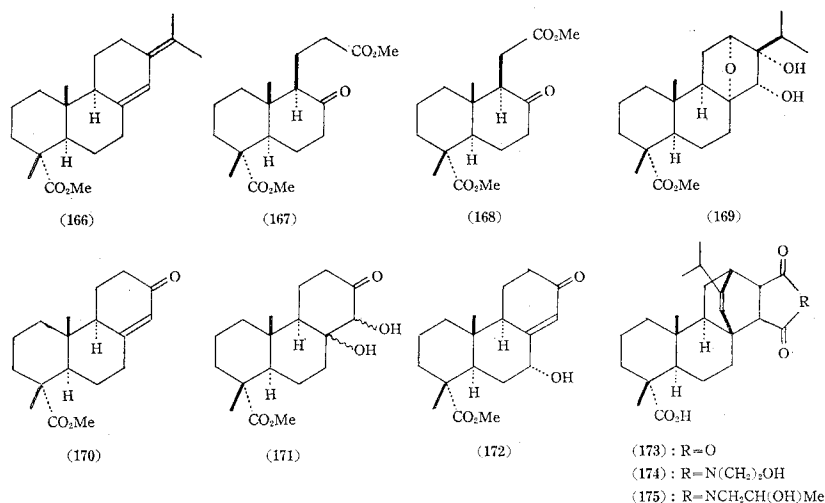


Chart 3

The major product from the solvolysis of the methyl bromoabietate formed by a reaction of methyl abietate (**162**) with NBS was methyl 12 α -methoxyabietate (**163**). The structure was proved by independent synthesis from 12 α -hydroxyabietic acid. Methyl 15-methoxyabietate (**164**) was also formed. The three possible methyl methoxydehydroabietates were obtained as secondary reaction products from the methyl dehydroabietate (**165**) formed during the NBS-abietate reaction. They were also prepared by the solvolysis of NBS-methyl dehydroabietate reaction products. The main parts of the sequences are given in Chart

4.⁶⁴⁾

Lemieux oxidation of 166 afforded 167 in 50% yield, but the Lemieux oxidation of 141a gave varying yields of 168 and 169. Procedures for the exhaustive ozonolysis of 166 and 141a were standardized to afford the important synthetic intermediates, 167 and 168, in 55~60% yields. Partial ozonolysis of 166 afforded 170, 171, and 172. Oxidation of 170, 166, and 141a with $\text{RuO}_4\text{-NaIO}_4$ followed by esterification gave 167, 167, and 168 in excellent yields.⁶⁵⁾



N-(Hydroxyalkyl)-maleimidopimamic acids were synthesized. Compound 173 was refluxed with β -hydroxyethylamine in methanol to give 174, while it was heated at 120° with β -hydroxy-n-propylamine in dimethylformamide to afford 175. Several metallic salts of 174 were prepared. Compounds 174 and 175 are polymer

intermediates.⁶⁶⁾

Podocarpic acid (14) was converted into taxodione (176) *via* a route shown in Chart 5. Since the total synthesis of the former has been recorded, this conversion implies a formal total synthesis of the latter.⁶⁷⁾

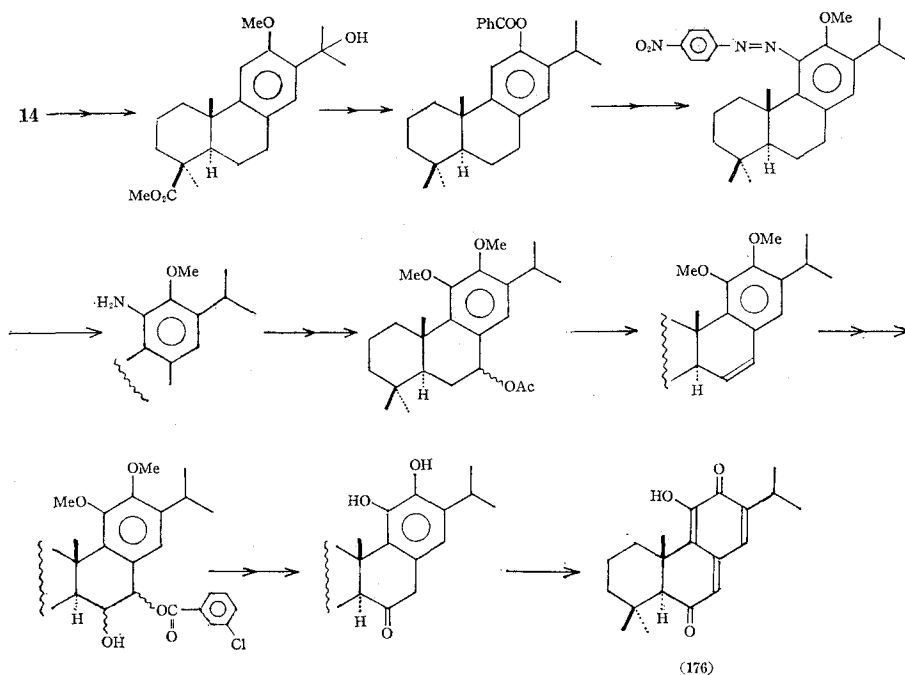
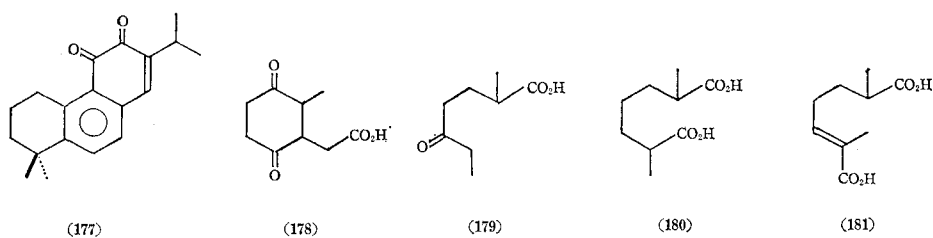


Chart 5

From the roots of *Salvia miltiorrhiza*, a new red crystalline pigment, miltirone (177), was isolated and characterized.⁶⁸⁾

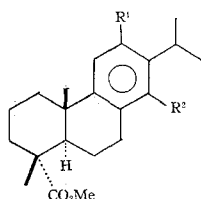


Microbial degradation of dehydroabietic acid was investigated. Degradation products 178 and 179 by *Flavobacterium resinovorum* and 180 and 181 by *Pseudomonas resinovorans* were isolated and characterized as their methyl esters.⁶⁹⁾

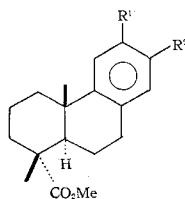
Nitration of methyl 12-acetylabieta-8, 11, 13-trien-18-oate (182) gave the products 183 and 184, and the latter was converted into methyl 13-hydroxypodocarpa-8, 11, 13-trien-18-oate (185) in 26% overall yield from methyl abieta-8, 11, 13-trien-18-oate (methyl dehydroabietate).⁷⁰⁾

When methyl neoabietate (166) was photolyzed in methanol with a low pressure mercury lamp, the only solid methoxy compound obtained was shown to

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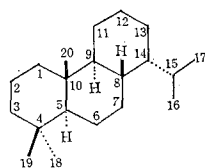
(182) : $R^1 = \text{Ac}, R^2 = \text{H}$
 (183) : $R^1 = \text{NO}_2, R^2 = \text{NO}_2$



(184) : $R^1 = \text{Ac}, R^2 = \text{NO}_2$
 (185) : $R^1 = \text{H}, R^2 = \text{OH}$

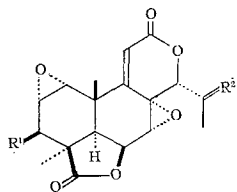
be 164.⁷¹⁾

VII. TOTARANE DERIVATIVES



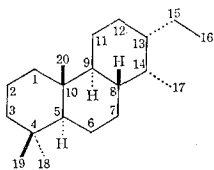
Totarane

From the extract of the bark of *Podocarpus* species (cf. *P. neriifolius*), podolactone-A and -B, which strongly inhibit expansion and mitosis of plant cells, were isolated as crystals and structures 186 and 187 were assigned to A and B, respectively.⁷²⁾



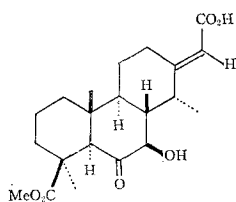
(186) : $R^1 = \text{H}, R^2 = \text{OH}, \text{CH}_2\text{OH}$
 (187) : $R^1 = \text{OH}, R^2 = \text{OH}, \text{CH}_2\text{OH}$

VIII. CASSANE DERIVATIVES

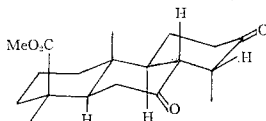


Cassane

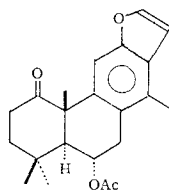
Structure 188 was suggested for cassminic acid, a minor constituent from the bark of *Erythrophleum guineense*.⁷³⁾ The assignment of the 14-methyl group in cassamic acid and its congeners (e.g. 189) to the axial conformation was supported by the experimental results. Magnetic anisotropy calculation was also in agreement with this assignment.⁷⁴⁾



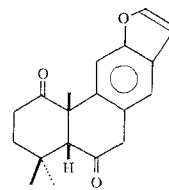
(188)



(189)



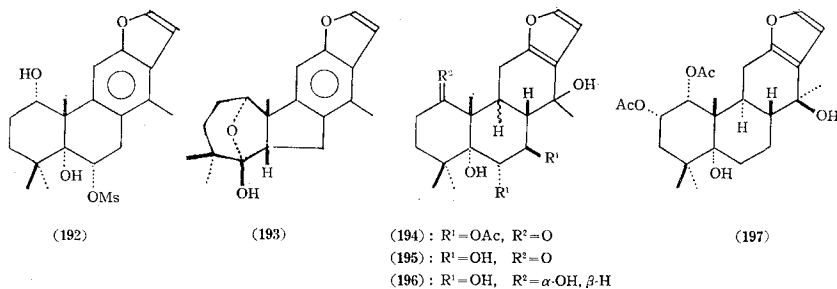
(190)



(191)

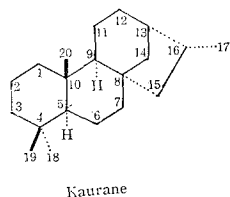
Under the conditions of the Serini reaction, the benzofuran 190 derived from α -caesalpin rearranged to the diketone 191 with a *cis*-A, B ring-junction, while on mild base treatment the benzofuran mesylate 192 from δ -caesalpin underwent

a pinacol-type rearrangement to the hemiacetal **193**. On the basis of consideration of steric course of these reactions, in conjunction with other evidence, the relative stereochemistry of α -, β -, and δ -caesalpins was assigned as in **194**, **195**, and **196**, respectively.⁷⁵⁾

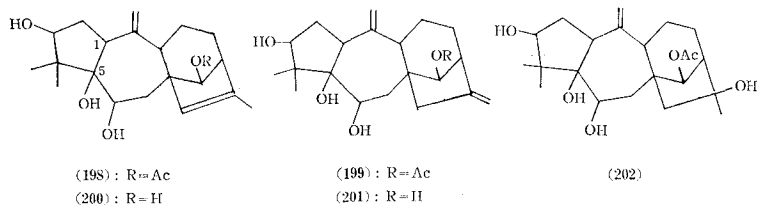


From the bark of *Caesalpinia pulcherrima*, a new cassane derivative named x-caesalpin was isolated. Structure **197** was proposed for this compound.⁷⁶⁾

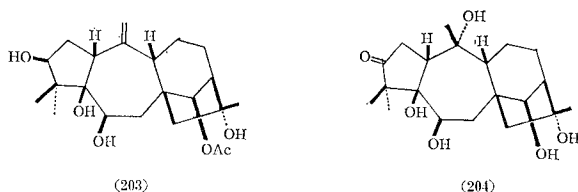
IX. KAURANE DERIVATIVES*



A mixture of two grayanotoxin acetates **198** and **199**, was isolated from older extracts of leaves from *Rhododendron ponticum*. The corresponding alcohols, **200** and **201**, were also chromatographically detectable in these extracts. Very probably, a $1\alpha, 5\beta$ -configuration was assigned.⁷⁷⁾ Another grayanotoxin **202** was isolated from the leaves of the same plant.⁷⁸⁾



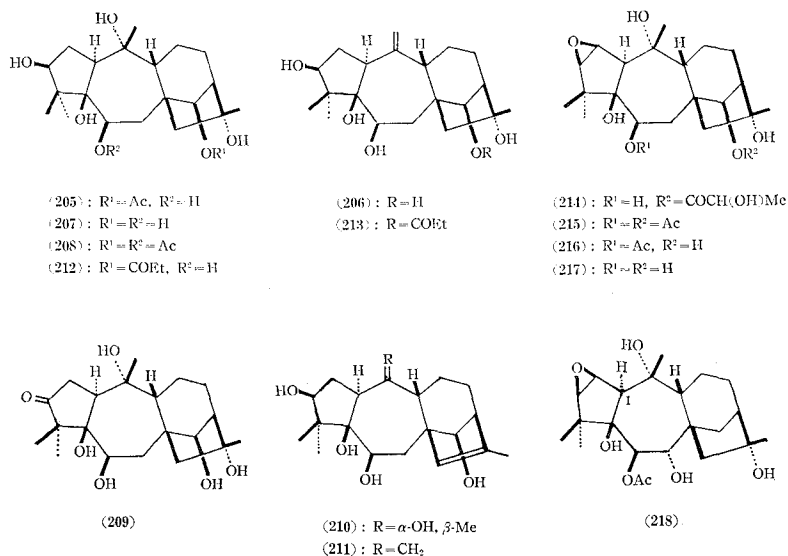
Two physiologically active diterpenoids, grayanotoxin-IV and -V, were isolated from *Leucothoe grayana*. The structures including absolute configurations **203** and **204** were supplied respectively.⁷⁹⁾



* See also section III, ref. 22, section V, ref. 43, and section X, ref. 120.

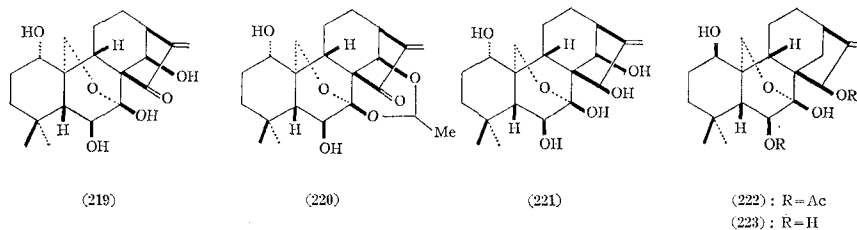
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The stereochemistry of grayanotoxins, asebotoxins, and rhodojaponins, toxins of Ericaceae, however, was revised to C-1 α and C-5 β configuration (A/B *trans*) by several groups.^{80,81,83,84,85)} Revised structures are as follows: grayanotoxin-I (205), -II (206), -III (207), -IV (208), -V (209), -VI (210), -VII (211), asebotoxin-I (212), -II (213), -III (214), rhodojaponin-I (215), -II (216), and -III (217). An x-ray analysis of grayanotoxin-I gave a confirmative evidence.⁸⁶⁾



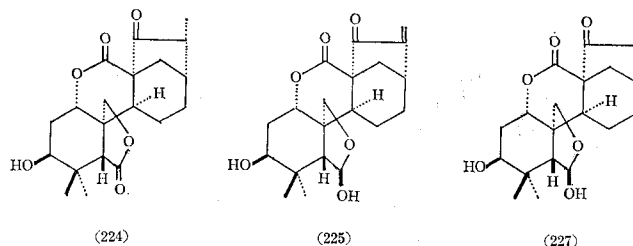
The structure and stereochemistry of lyoniatoxin, a toxin of *Lyonia ovalifolia*, were investigated, and formula 218 was assigned to this substance,⁸²⁾ while the A/B *cis*-junction with C-1 β H in 218 was assigned to the same compound named lyoniol A by another group.^{87,88)}

Isolation of new constituents from *Isodon trichocarpus* and the structures, 219, 220, and 221, of isodonol, enmedol, and enmenol were reported.⁸⁹⁾ Isodonol is identical with oridonin elucidated already by the author *et al.*⁹⁰⁾



The structures of enmenin, enmelol, and ememodin, isolated from *Isodon trichocarpus*, were determined to be 222, 223, and 224, respectively.⁹¹⁾ Enmenin is the same compound as trichokaurin whose structure and absolute configuration has been established by the author *et al.*⁹²⁾

The full paper on the formal conversion of enmein (225) into *ent*-kaurene, atisine, garryine, and veatchine was published.⁹³⁾ The preliminary communi-



cation had been published and the more detailed explanation had been done in the preceding number⁶⁾ of this series of reviews.

The full paper on the structure and absolute configuration of oridonin (219) isolated from *Isodon japonicus* and *I. trichocarpus* was also published.⁹⁴⁾

Oridonin (219) was transformed into isodocarpin (226) via a route shown in Chart 6.⁹⁵⁾ Similarly, dihydroenmein (227) was also converted into enmein (225).

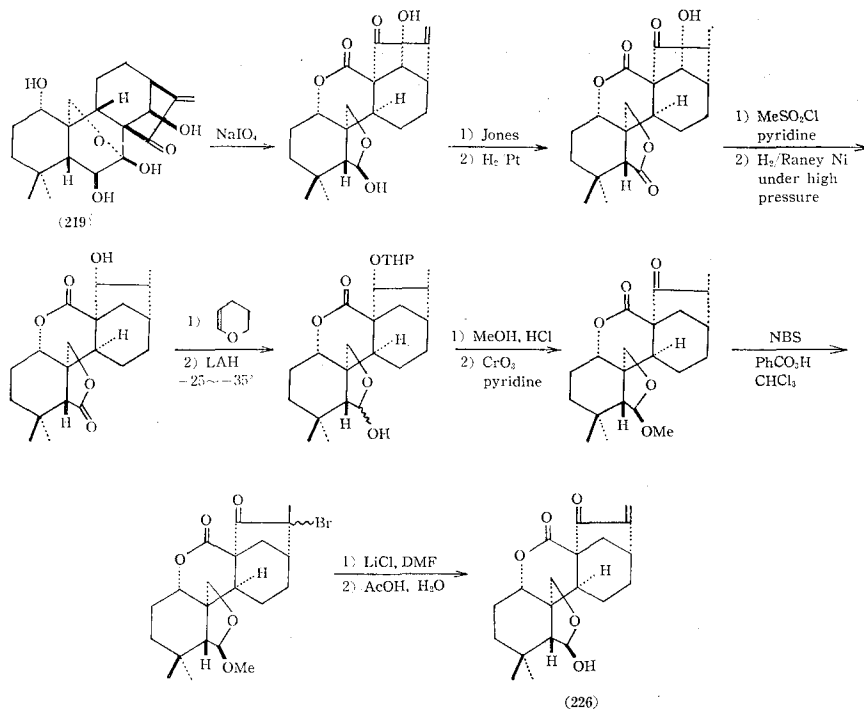


Chart 6

Previously, trichokaurin (222) had been converted into dihydroisodocarpin,⁹²⁾ and the latter has been transformed into isodocarpin (226).⁹⁵⁾ Thus, a chemical conversion of trichokaurin into isodocarpin has been accomplished. Now, a more convenient and shorter route was developed, as shown in Chart 7.⁹⁶⁾

All the published syntheses in the diterpene alkaloid series had involved the total synthesis of a racemic intermediate, the correlation of this material with an optically active degradation product of the same structure and finally the conversion of this optically active relay compound to the optically active alkaloid. Wiesner *et al.*⁹⁷⁾ resolved the synthetic racemic compound (as 228) into

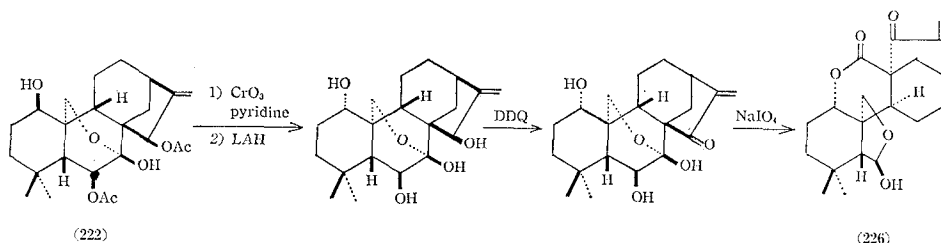
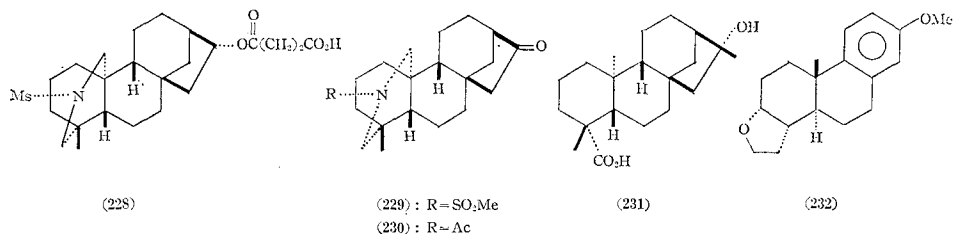


Chart 7

optically active enantiomers and converted each enantiomer into the ketone. One of them was proved to be identical with degradation product 229 from natural alkaloid. This enantiomer was converted into N-acetate 230, which had been converted into garryine and veatchine by themselves. Thus, the total synthesis of the natural optically active form of these alkaloids was complete.



A diterpene acid was isolated from *Enhydra fluctuans*; its properties and spectral data, and its dehydration with phosphoryl chloride and pyridine, or refluxing with acetic anhydride and pyridine to *ent*-kaur-16-en-19-oic acid led to its identification as *ent*-16 β -hydroxykauran-19-oic acid (231). The latter was prepared by hydration of the former.⁹⁸⁾

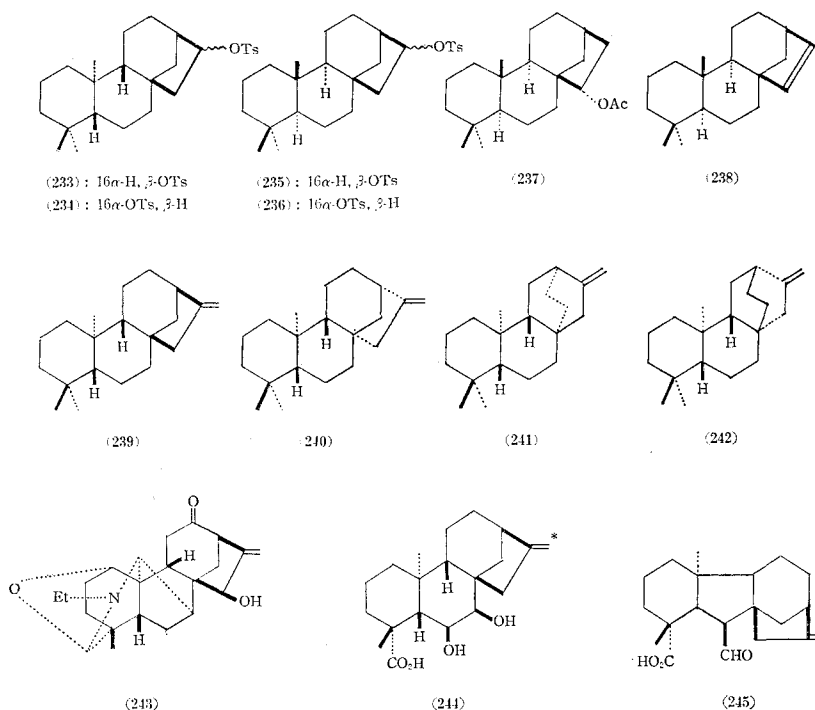
The synthesis of 232, a cafestol intermediate was reported.⁹⁹⁾

The *ent*-norkauranol tosylates 233 and 234 each furnished six acetates and three olefins on buffered acetolysis. The equivalent norphyllocladanol tosylates 235 and 236 gave the enantiomers of these six acetates, one additional acetate 237, and only one olefin 238. These transformations provided a route for the conversion of *ent*-16-kaurene (239) into *ent*-phyllocladene (240), atisirene (241), and neoatisirene (242) and could in principle be utilized for the formation of kaurene, *anti*-atisirene, and *anti*-neoatisirene from phyllocladene. Mechanistic aspects of the solvolysis were discussed: in particular, a pathway, which included a 1,2-hydride shift from C-15 to C-16, was tentatively suggested as a rationalization of the high yield of 238 from 236.¹⁰⁰⁾

Aconitine, songorine, and songoramine were isolated from *Aconitum karakolicum*. UV, IR, NMR, and mass spectral analyses suggested structure 243 for songoramine.¹⁰¹⁾

The mass spectra of *ent*-kauran-16-ols were reported.¹⁰²⁾ These compounds differ either by stereochemistry at C-16 or in the substituent at C-4. In all cases, the most characteristic ions corresponded to a loss of ring D as a C₈H₈O fragment. The substituent R at C-4 was deduced from such typical ions as [M-R]⁺

Chemistry on Diterpenoids in 1970



or $[M-R-H_2O]^+$. Kauranols epimeric at C-16 showed little difference in their mass spectra; the assignment of configuration at this center requires the spectra of both epimers.

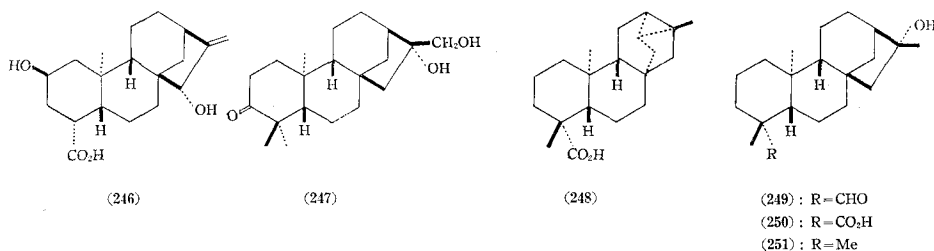
ent-Kauran-16-ol and *ent*-16-kahren-19-oic acid were isolated from *Enhydra fluctuans*.¹⁰³⁾ Diterpenes from the leaves of *Cryptomeria japonica* were investigated. Consequently, *C. japonica* trees were sub-divided into four chemically distinct varieties on the basis of the diterpene hydrocarbon content of their leaves. Seven other species from the Taxodiaceae were analyzed for diterpenes.¹⁰⁴⁾

$[17-^{14}C]$ -*ent*-6 α ,7 α -Dihydroxy-16-kahren-19-oic acid (244) was prepared and fed to *Gibberella fujikuroi*. It was not useful as the precursor of gibberellic acid, but was incorporated into fujenal. However, dilution analysis showed the dihydroxy acid 244 to be a metabolite of *G. fujikuroi*, and the acid was shown to be more active than kahrenoic acid and dehydro acid 245 in four bioassays to gibberellins. Thus, a possibility that a derivative of dihydroxy acid 244, *e.g.* a 6-pyrophosphate, could be a precursor of gibberellins can not be excluded, according to Cross and Stewart.¹⁰⁵⁾

The complete configuration 246 of atractyligenin was obtained by a three-dimensional single-crystal x-ray diffraction study of epoxybromoatractyligenin.¹⁰⁶⁾

The complete structure 247 of abbeokutone was presented.¹⁰⁷⁾ It was identical with the previously assigned structure. A new trachylobane derivative 248 together with the biogenetically related *ent*-16-kahren-19-oic acid was isolated from the flowers of *Helianthus annuus*.¹⁰⁸⁾

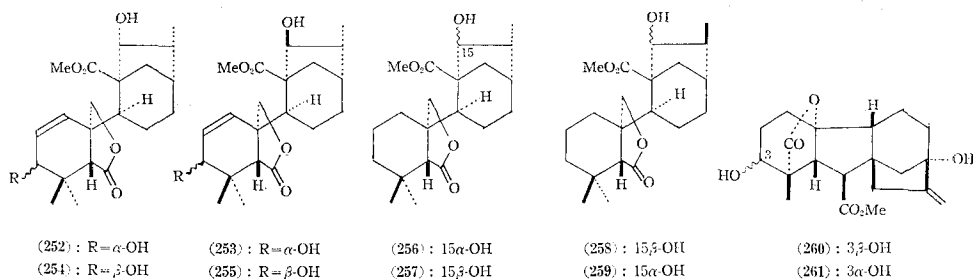
Culture filtrates of *Fusarium moniliforme* was shown to contain *ent*-16 β -



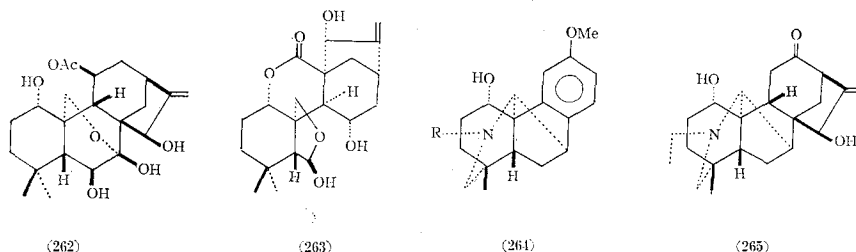
hydroxykauran-19-al (249) and *ent*-16 β -hydroxykauran-19-oic acid (250)—two diterpenoids related to the intermediates in the biosynthesis of gibberellins.¹⁰⁹⁾

ent-Kauran-16 β -ol (251) was isolated from *Anthelia julacea* and *A. juratzkana*.¹¹⁰⁾

It was observed that a common stereoelectronic requirement is satisfied in the epimerization by weak alkali of the *cis*-alcohols, 252, 254, 256, and 258, into the *trans*-epimers, 253, 255, 257, and 259, respectively and also in the epimerization of the β -axial alcohol 260 of the gibberellin series into its α -equatorial epimer 261.¹¹¹⁾



Structures 262 and 263 were assigned to sodoaponin and epinodosinol, respectively, new minor diterpenoids of *Isodon japonicus*.¹¹²⁾



Several approaches to further development of intermediate 264 to songorine 265 were tested. In a communication,¹¹³⁾ a simple and stereoselective new method of conversion of phenol 266 into two tetracyclic diketones 267 and 268. The outline is shown in Chart 8.

The metabolites from the succinate ester (269) of *ent*-16-kauren-19-ol in *Gibberella fujikuroi* were investigated and, diol 270 and triol 271 were isolated in 12 and 20% yields, respectively, after hydrolysis of acidic fraction.¹¹⁴⁾

Chemistry on Diterpenoids in 1970

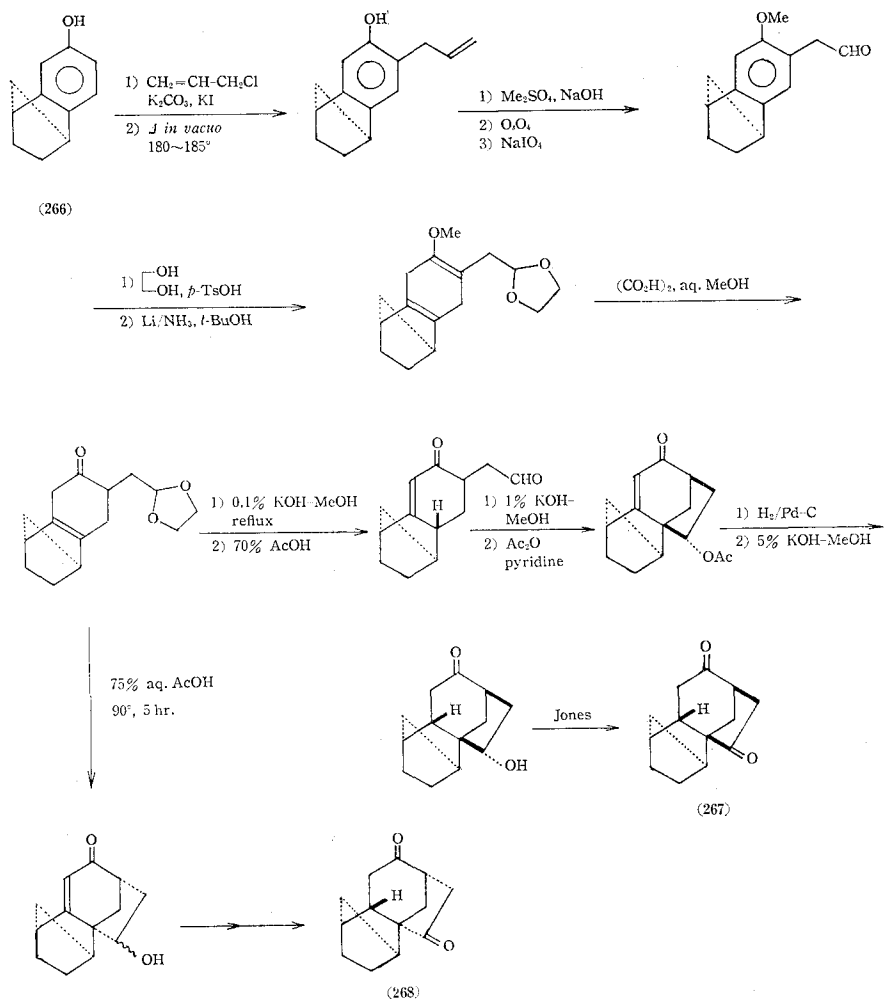
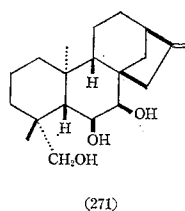
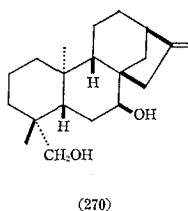
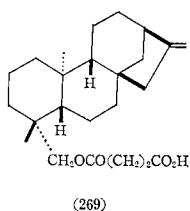


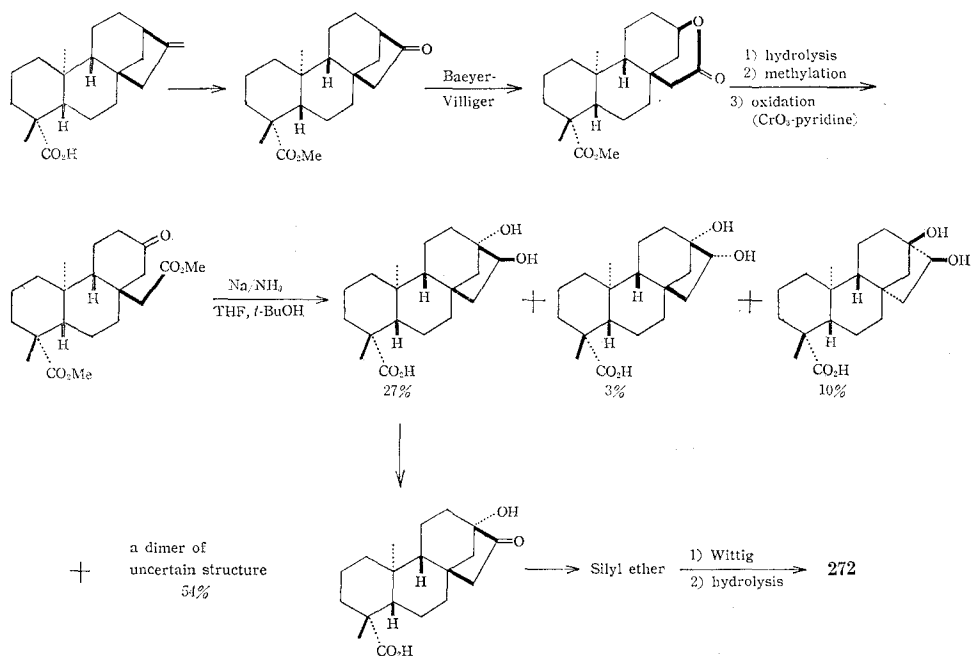
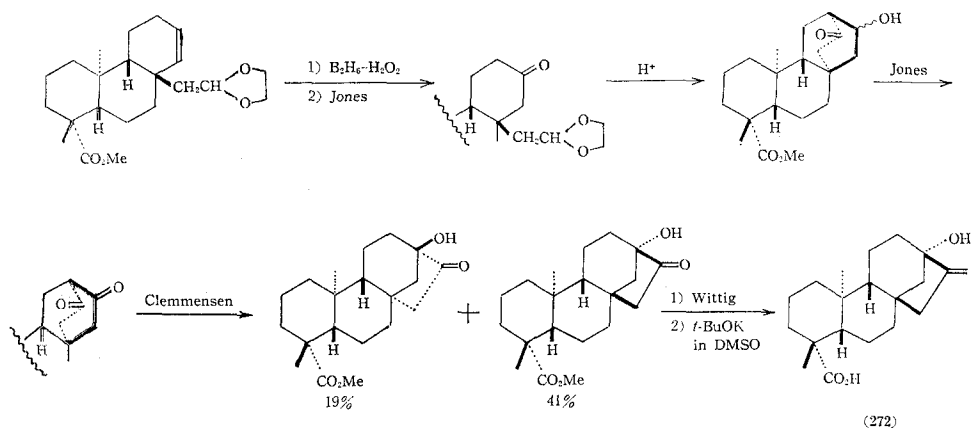
Chart 8



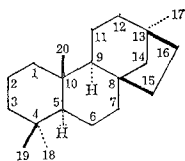
Syntheses of steviol (272), the aglucon of stevioside, the remarkably sweet glucoside abundant in *Stevia rebaudiana*, were carried out by two groups. A Japanese group¹¹⁵⁾ synthesized *rac*-steviol following the route shown in Chart 9.

Australian group¹¹⁶⁾ synthesized optically active steviol following the route shown in Chart 10.

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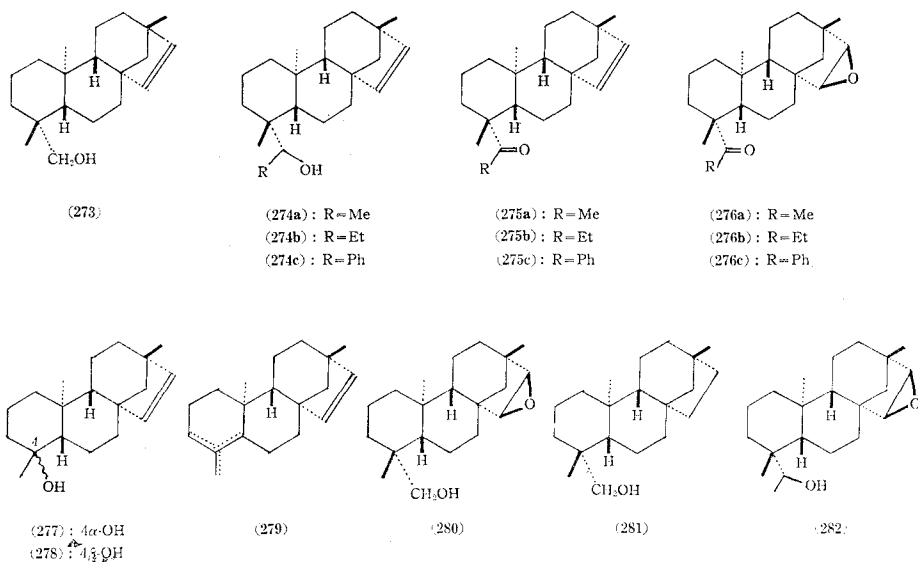
X. BEYERANE DERIVATIVES*



Unusual oxidations had been reported on erythrolyol A(273).¹¹⁷⁾ Now, other related compounds were investigated. Derivatives 274 a, b, c were oxidized by chromic anhydride in aqueous acetic acid to yield 275 a, b, c and 276 a, b, c as major products and 277 to 279 as minor products. Oxidations of compounds 280, 281, and 282, were checked, and

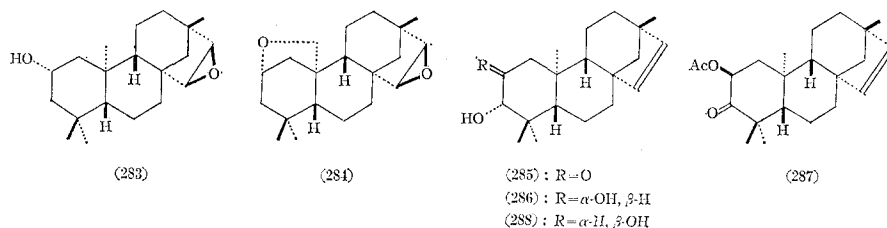
* See section V, ref. 46.

Chemistry on Diterpenoids in 1970

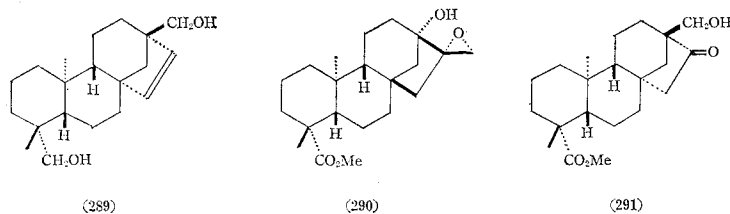


mechanism for formation of 18- or 19-nor-products was suggested.¹¹³⁾

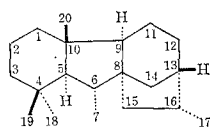
ent-15-Beyeren-2 β , 3 β , and 3 α -alcohols were prepared, and their stereochemistry assigned. *ent*-2 β -Hydroxybeyer-15, 16-epoxide (283) underwent reaction with lead tetraacetate to form a 2-20 ether 284 which could be rearranged to a kaurenoid skeleton. Reduction of *ent*-3 β -hydroxy-15-beyeren-2-one (285) afforded 2 α , 3 α -diol 286. Treatment of the 3-monotosylate of the diol with alumina afforded the 2-ketone. 15-Beyeren-3-one underwent acetoxylation to furnish the corresponding 2 β -acetate 287 which was reduced to a 2 β , 3 α -diol 288. The solvent shifts in the NMR spectra of these compounds were studied.¹¹⁹⁾



Steviol (272) was converted into erythroxydiol A (289) *via* an acid-catalyzed rearrangement from 290 to 291.¹²⁰⁾

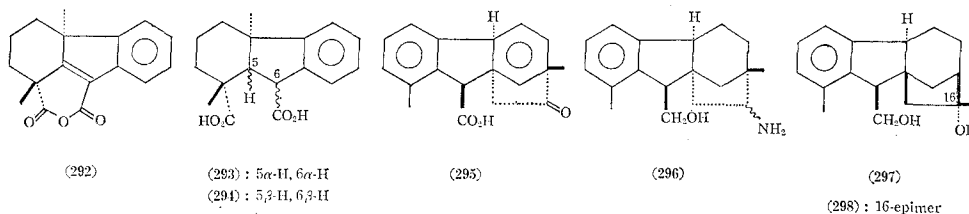


XI. GIBBERELLANE DERIVATIVES*



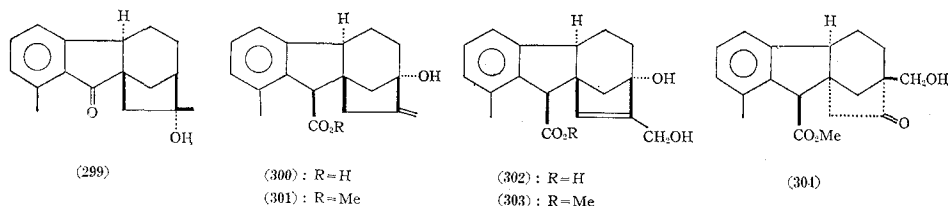
Gibberellane

Hexahydrofluorene derivatives, 293 and 294, were synthesized *via* an intermediate 292 from abietic acid. Compounds 293 and 294 were converted into methyl esters, and the latter compounds were transformed into all the remaining C-5, C-6 epimers of free acid and ester.¹²¹⁾

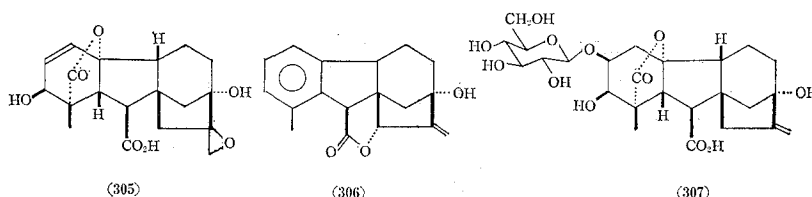


Epoxidation and hydration of an unsaturated keton of the gibberellin series were investigated.¹²²⁾

Gibberic acid (295) was converted into amine 296, which was deaminated to give 297 accompanied by 16-epimer 298. Oxidation of 297 gave the expected acid in addition to unexpected 6-ketone 299.¹²³⁾



Attempts to photo-oxygenate the 2,3-and 16,17-double bonds in some derivatives of *ent*-gibberellane were unsuccessful except in the case of allogibberic acid (300) and its methyl ester (301), which reacted at the 16,17-double bond to give the expected 15-en-17-ols, 302 and 303, respectively. Acid-catalyzed rearrangement of 303 gave the hydroxymethyl derivative 304 of methyl gibberate, which was identical with the methyl ester of the rearranged product obtained from gibberellin-A₃ 16,17-epoxide (305) at 100° in 2N-HCl. The major product from the rearrangement (treatment with 2N HCl) of the product (303) of photo-oxygenation of methyl allogibberate (301) was the 7,15-olide 306 of 15-hydroxyallogibberic acid.¹²⁴⁾



* See section IX, refs. 105, 109, and 111.

The stereoselective labelling of the gibberellins and the kaurenolides with 2-(R)-, 2-(S)-, and 5-(R)-[^3H] mevalonate was studied. The results led to the conclusion that the dehydrogenation of ring A in gibberellic acid biosynthesis is a *cis*-process and that the hydroxylation of ring B in the formation of the kaurenolides takes place with retention of configuration. One tritium atom from [$1\text{-}^3\text{H}$, $2\text{-}^{14}\text{C}$] geranyl pyrophosphate was retained at position 6 in gibberellic acid. However, 5-(R)-mevalonoid hydrogen was lost from ring B during the formation of the gibberellins. Consequently, ring contraction took place with the displacement of an equatorial hydrogen atom from kauranoid C-6 position.¹²⁵⁾

From fresh immature fruits of *Phaseolus coccineus* a polar gibberellin (previously named "Phaseolus ϵ ") was isolated in an overall yield of $3.8 \times 10^{-5} \%$. Its structure was shown by chemical and physical methods to be gibberellin A₈-O(2)- β -glucopyranoside (307).¹²⁶⁾

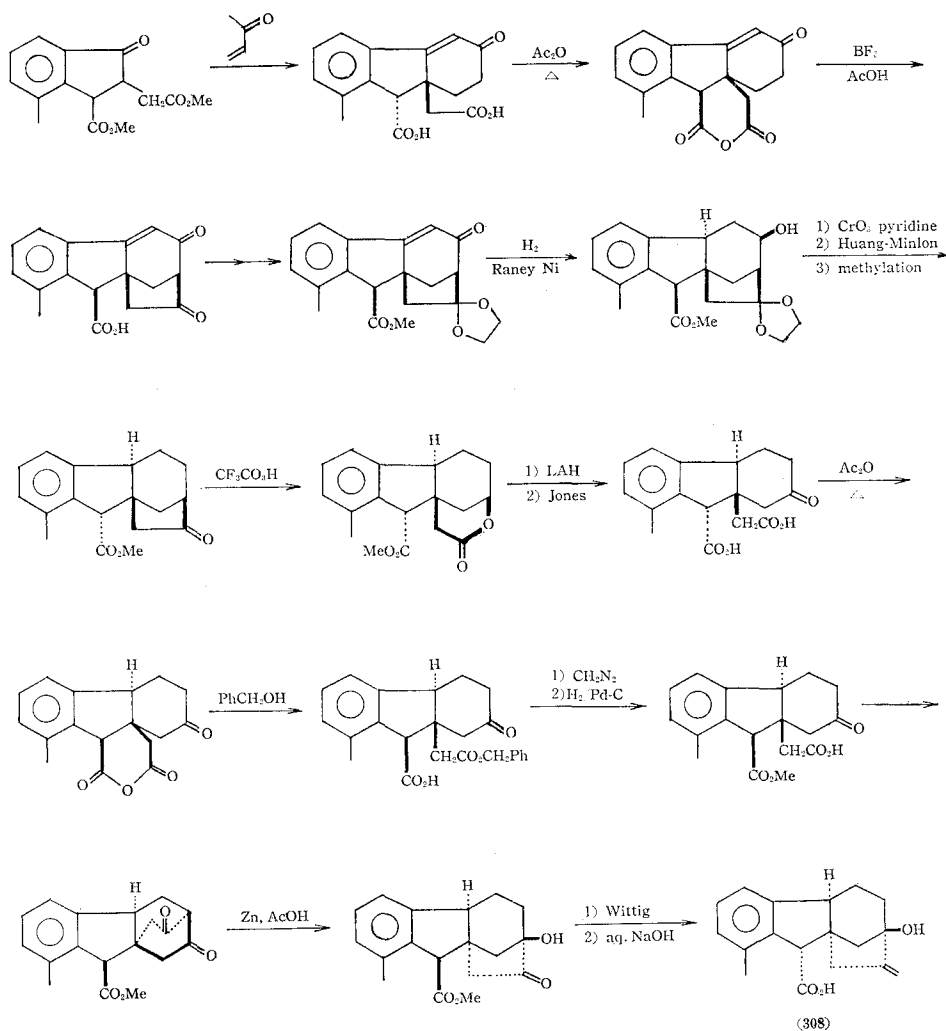


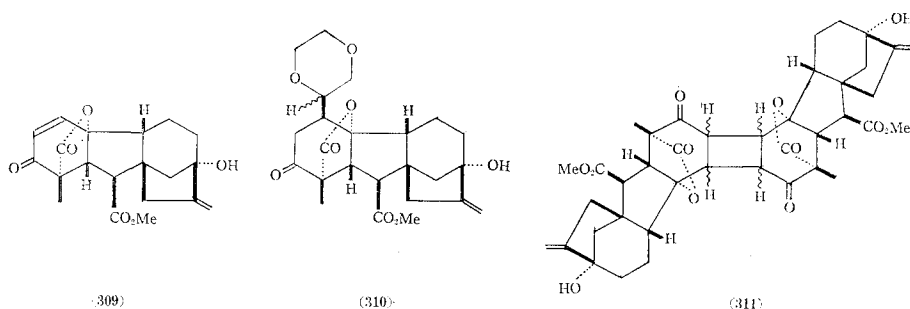
Chart 11

The presence of gibberellic acid (GA_3) in the petals and stamens of *Cassia fistula* was reported on the basis of chromatography, bioassays, spectrofluorometry, superimposed IR spectrum and mass fragmentation pattern.¹²⁷⁾

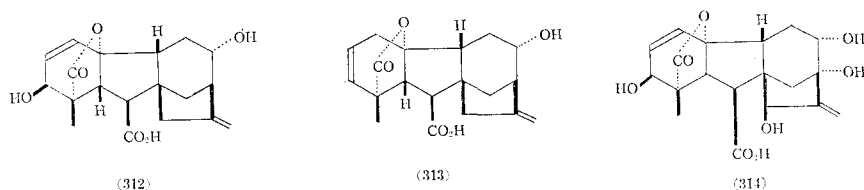
A total synthesis of *rac*-epiallogibberic acid (as 308) was reported. The route is shown in Chart 11.^{128,129)}

A list of references for physiologically active substances of plants including gibberellins was published in Japanese.¹³⁰⁾

A photochemical behavior of the α, β -unsaturated ketone 309 derived from gibberellin A_3 in absolute dioxane was investigated. The products were shown to be an adduct 310 and a dimer 311.¹³¹⁾



From immature seeds of *Calonyction aculeatum*, twelve gibberellins (or methyl esters) were isolated and five of them were identified as known gibberellins, namely GA_8 , GA_{17} , GA_{19} , GA_{27} , and GA_{29} , by melting points, gas chromatography, IR, and mass spectra. The other gibberellins were shown to be new ones. Structures of two of them, named GA_{30} and GA_{31} , were determined, that is, structure 312 was assigned to GA_{30} , while 313 to GA_{31} .¹³²⁾



A new water-soluble gibberellin (GA_{32}), which is not gibberellin glucoside, was isolated from immature seeds of *Prunus persica*, and its structure was determined as 314.¹³³⁾

Partial synthesis of gibberellin A_{15} norketone (316) from 7-hydroxykaurenolide (315) was reported,¹³⁴⁾ as shown in Chart 12.

Gibberellin- A_{15} (317) was derived from enmein (225) *via* a route shown in Chart 13.¹³⁵⁾

The stereocontrolled total synthesis of racemic gibberellin A_{15} (317) was accomplished.¹³⁶⁾ The route is shown in Chart 14.

As an approach to the total synthesis of gibberellic acid, a simple route to

Chemistry on Diterpenoids in 1970

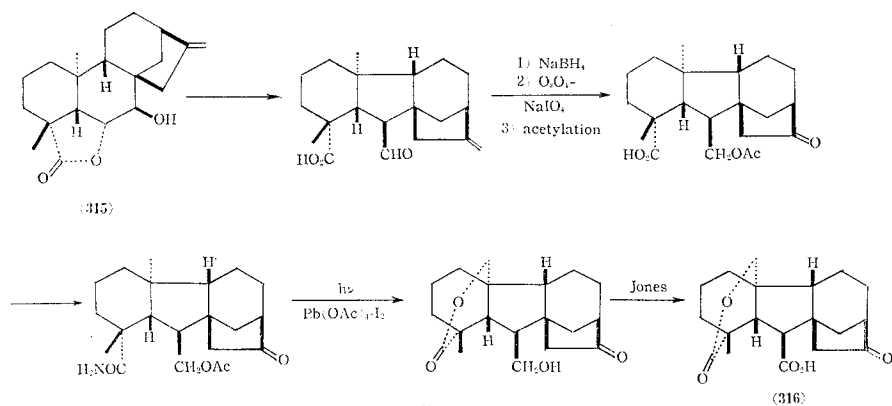


Chart 12

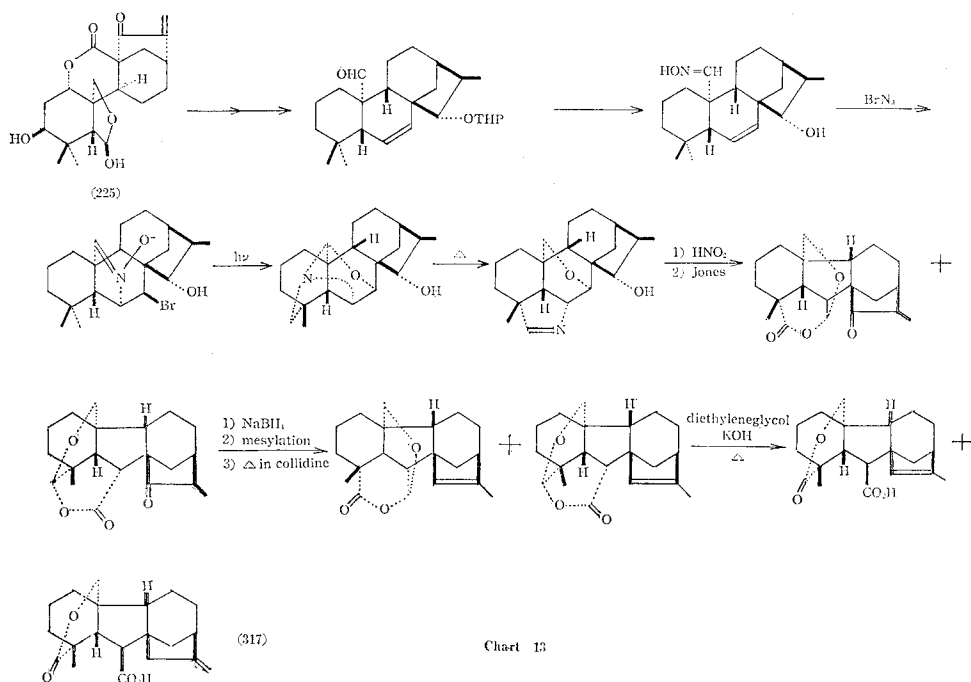


Chart 13

tetracyclic network was developed,¹³⁷⁾ as shown in Chart 15.

Tetrahydro-derivative of gibberellic acid was isolated from leaves of *Sonneratia apetala*.¹³⁸⁾ Gibberellin A₂₅ was used for this compound, but gibberellin A₂₅ had been allocated to the metabolite 318 from *G. fujikuroi*. To remove all ambiguity it was hoped that this name for the compound from *S. apetala* will be withdrawn.¹³⁹⁾

Structure 319 was assigned to a new gibberellin glucoside, which was tentatively termed F-VII in immature seeds of *Pharbitis nil*.¹⁴⁰⁾

The *cis*-1, 2, 3, 4, 4a, 9a-hexahydro-1-methyl-6-methoxy-9-oxofluorene-1-carboxylic acids 321 and 322, potential intermediates in the synthesis of gibberellins were

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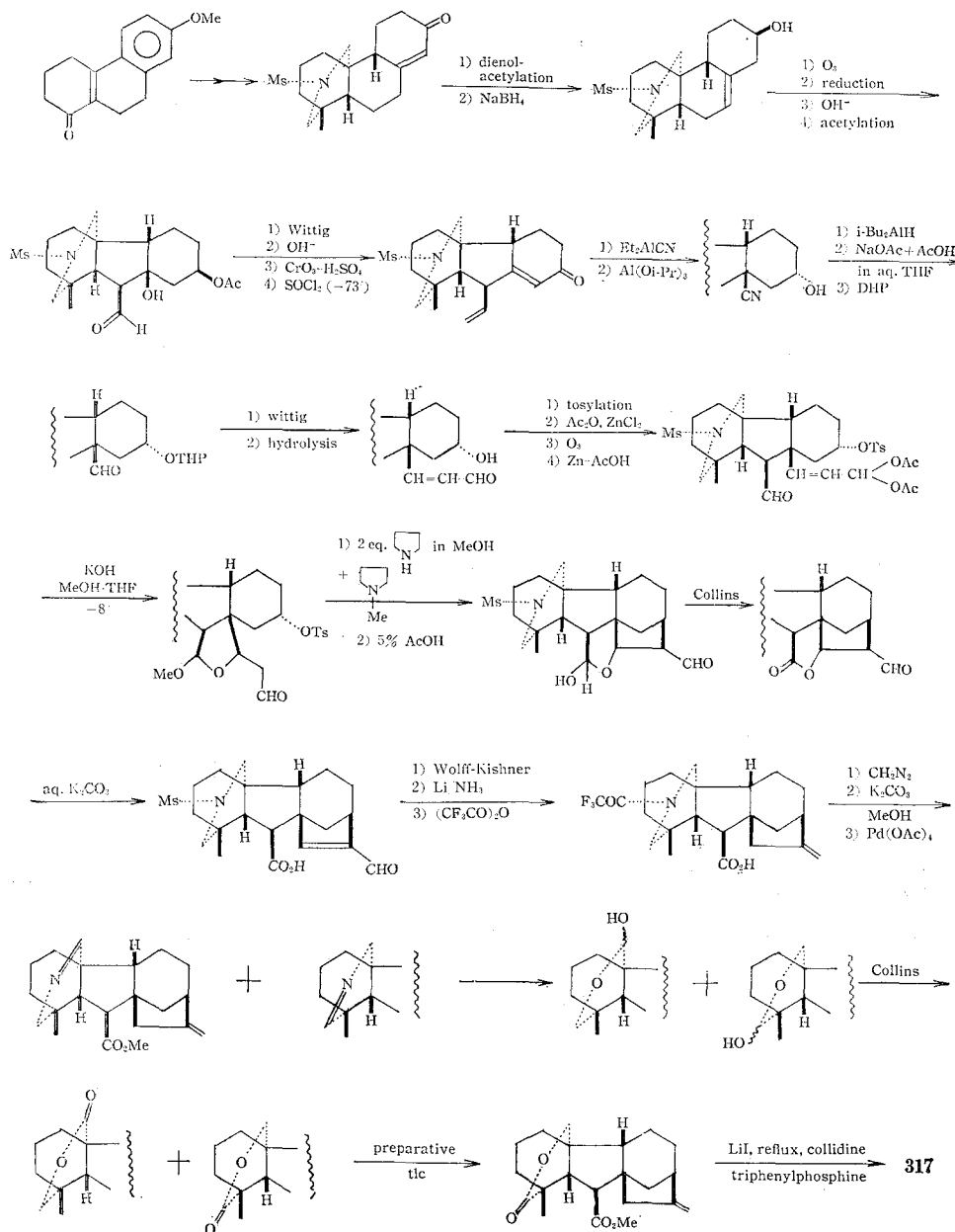


Chart 14

prepared in high yield by a novel photocyclization. The photolysis of 320, prepared from the Friedel-Crafts reaction between 1-methyl-2-cyclohexene-1, 2-dicarboxylic anhydride and anisole, gave a mixture of 321 and 322 in nearly quantitative yield.¹⁴¹⁾

Chemistry on Diterpenoids in 1970

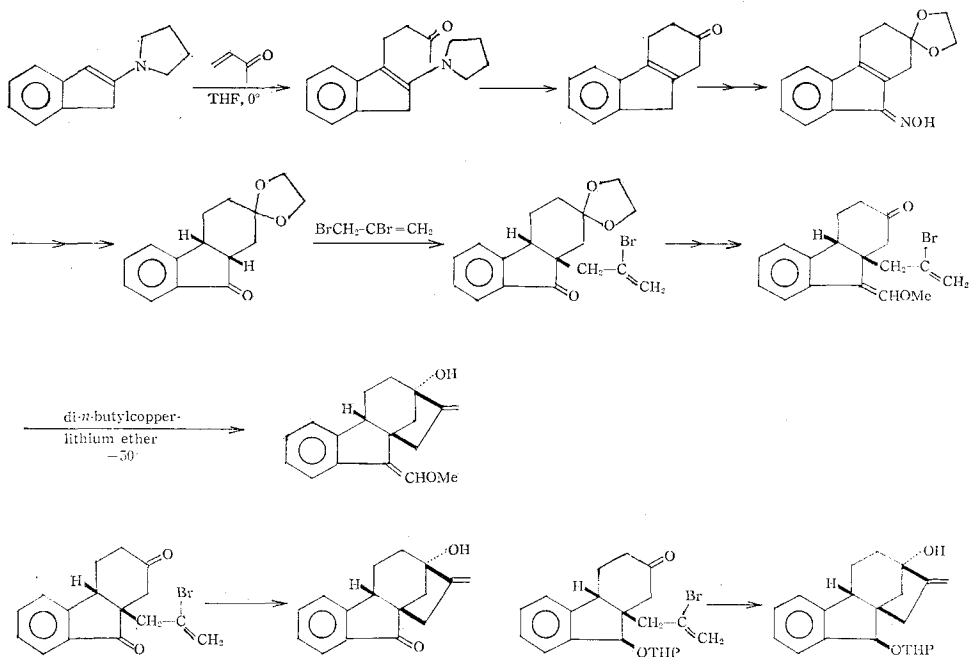
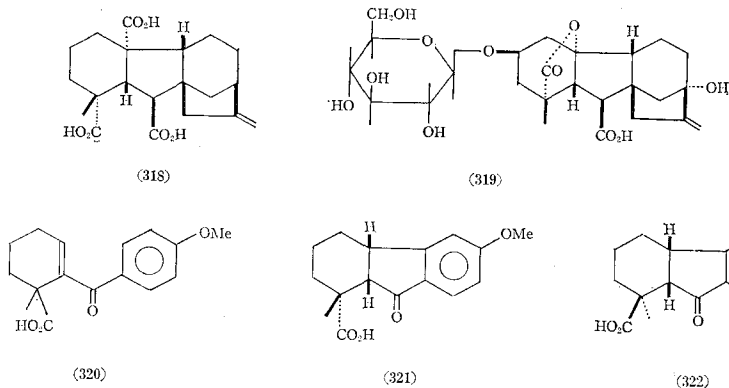
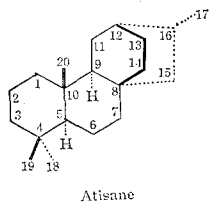


Chart 15



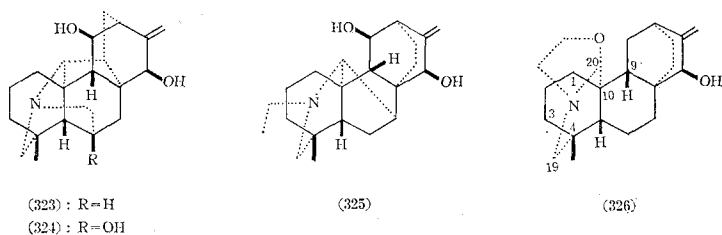
XII. ATISANE DERIVATIVES



The x-ray analysis showed that 323 is the correct stereochemical structure of kobusine, with both hydroxy groups having the β -configuration, and therefore, pseudokobusine is represented as 324.¹⁴²⁾ Another x-ray crystallographic determination of the structure 325 of denudatine was reported,¹⁴³⁾ which revised the previously assigned formula.

Atisine (**326**) in solution was shown to contain a 2:1 mixture of two isomeric species whose rate of interconversion is fast on the NMR time scale in polar

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hydrogen-bonding solvents, but relatively slow in solvents which would not stabilize an ionic species, leading to the suggestion that it is a mixture of configurational isomers at C-20 interconvertible *via* a zwitterion as shown in Chart 16.¹⁴⁴⁾

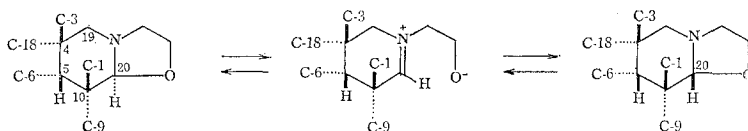
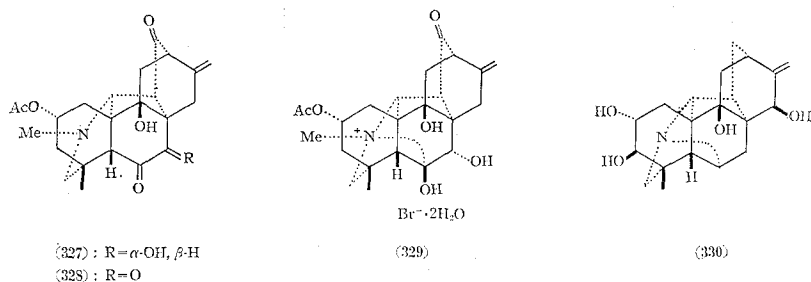


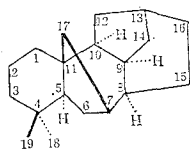
Chart 16

Miyaconitine and miyaconitinone, the major alkaloids from *Aconitum miyabei* were studied. On the basis of the chemical and spectral data found in continuing investigations as well as the biogenetical consideration, formulas 327 and 328 were shown to be most valid for these alkaloids.¹⁴⁵⁾ The x-ray determination of the structure 329 of miyaconitine hydrobromide dihydrate was also reported.¹⁴⁶⁾



The structure of anhydroignavinol, the alkaline hydrolysis product of ignavine, was investigated. Anhydroignavinol methiodide was prepared and subjected to a single-crystal x-ray analysis. The correct structure of anhydroignavinol was established as 330. The absolute configuration indicated was based on analogy with the other diterpene alkaloids.¹⁴⁷⁾

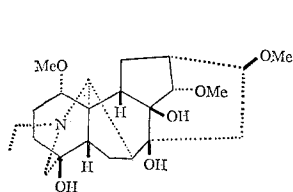
XIII. ACONANE DERIVATIVES



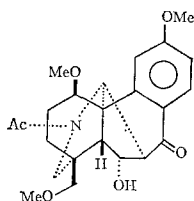
Aconane

The full paper of the crystal and molecular structure of lappaconine hydrobromide was published.¹⁴⁸⁾ The structure of lappaconine was shown to be 331.

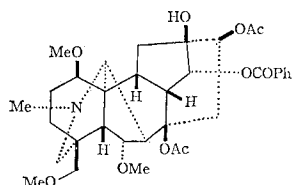
A stereoselective synthesis of an advanced relay compound for the total synthesis of delphinine (333) was



(331)



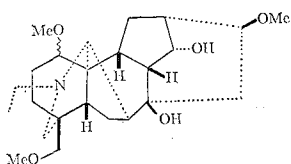
(332)



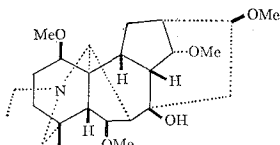
(333)

published.¹⁴⁹⁾ This compound 332, which has five rings and five substituents, is obtained easily from delphinine.

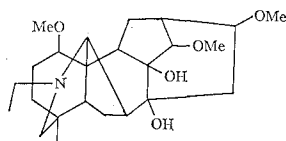
NMR and mass spectral investigation of talatisamine, its diacetyl, benzoyl, benzoylacetyl, and oxo-derivatives, and its pyrolytic products suggested the structure 334 for talatisamine.¹⁵⁰⁾



(334)

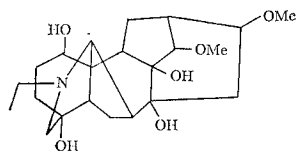


(335)

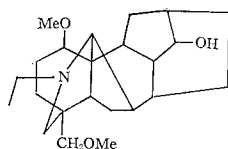


(336)

Delphatine, isolated from the seeds of *Delphinium biternatum*, was shown to have structure 335.¹⁵¹⁾ Lappaconitine, isolated from *Aconitum leucostomum*, was shown to have structure 336.¹⁵²⁾ Structure of lapaconidine extracted from *A. leucostomum* roots was shown to be 337.¹⁵³⁾



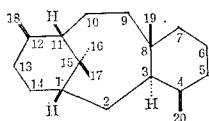
(337)



(338)

Pyrolysis of diacetylaltatisamine (diacetate of 334) in glycerol at 210-220° afforded 338 and a second unidentified product.¹⁵³⁾

XIV. TAXANE DERIVATIVES

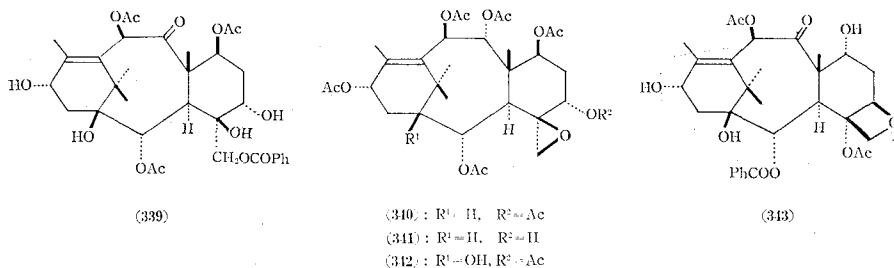


Taxane

The structure of baccatin-III isolated from *Taxus baccata* was shown to be 339.¹⁵⁴⁾ The signs of Cotton effects involving each of mono-olefinic centers of taxane derivatives were shown to be applicable to assignment of the absolute configuration of molecule.¹⁵⁵⁾

Baccatin-I isolated from the heartwood of *Taxus baccata* was shown to be 340. 5-Deacetylaltatisamine (341) and 1 β -hydroxybaccatin-I (342) were also isolated and characterized.¹⁵⁶⁾

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Baccatin-V, a new diterpenoid from *Taxus baccata* was shown by x-ray analysis to contain an oxetane ring and to be **343**.¹⁵⁷⁾ Its biogenesis was presented as shown in Chart 17.

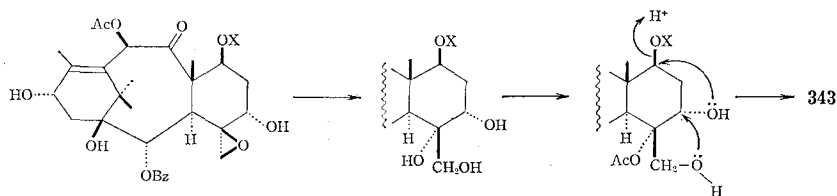
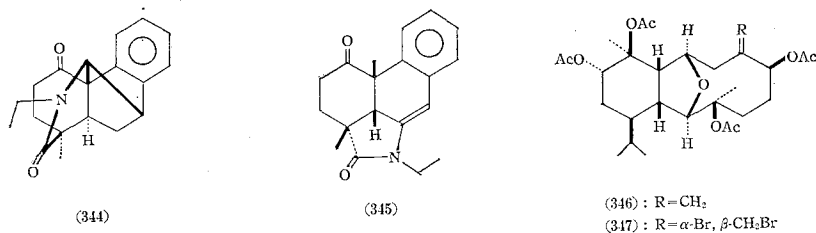


Chart 17

XV. THE OTHERS

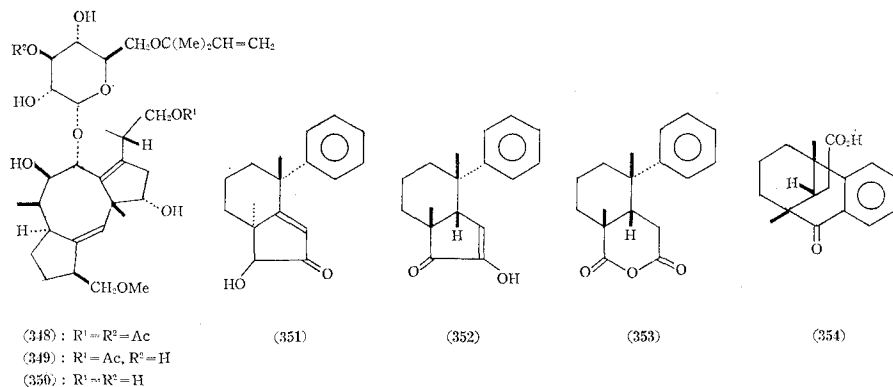
Wiesner and Ho attempted to prepare the lactam **344** and intended to use it as an intermediate for a synthesis of hexacyclic diterpene alkaloids. Although the material which they obtained gave the correct elemental analysis, its UV and NMR spectra did not agree with the proposed structure. This crystal structure determination, which was undertaken in order to establish unambiguously the structure of the synthetic intermediate, revealed the structure to be **345**. The synthesis of this compound and the results of this x-ray analysis had been published in a preliminary communication.¹⁵⁸⁾ Now, the full paper of this x-ray analysis was published.¹⁵⁹⁾



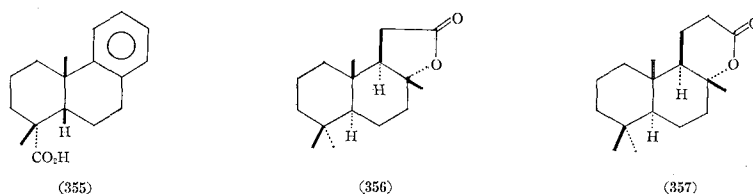
The structure **346** of eunicellin, a compound extracted from *Eunicella stricta* had been determined¹⁶⁰⁾ from the chemical evidence and an x-ray analysis of the dibromide derivative (**347**). Now, the full paper of this x-ray analysis was published.¹⁶¹⁾

By-products in culture filtrates of *Fusicoccum amygdali* were characterized.

Compound F III was shown to be an isomer of fusicoccin and named isofusicoccin. Quite possibly, the formation of isofusicoccin from fusicoccin (348) only involves a reversible rearrangement concerning the acetyl group present in the glucose moiety. Compound F IV was shown to be monodeacetylfusicoccin (349), while compound F VII was proved to be dideacetylfusicoccin (350).¹⁶²⁾



The base-catalyzed rearrangement of the unsaturated hydroxy ketone 351 was shown to generate the diosphenol 352 in virtually quantitative yield. Oxidation of 352 and then polyphosphoric acid catalyzed cyclization of the resulting anhydride 353 produced 354, but no 355. The driving force of the rearrangement reaction was discussed in terms of the steric crowding in the hydroxy ketone 351.¹⁶³⁾

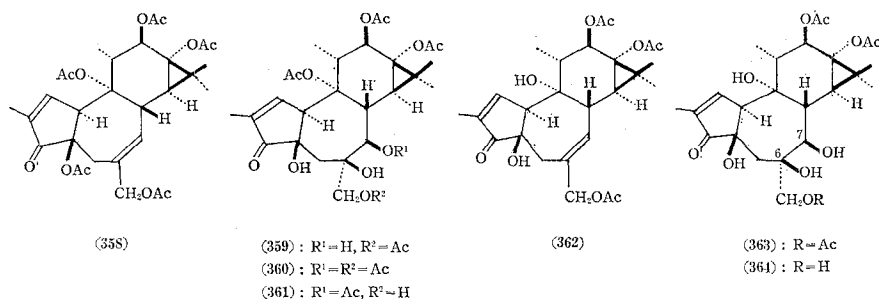


The main diterpenoid constituents of the oleoresin of *Pinus koraensis* were investigated.¹⁶⁴⁾ Diterpenoids from oleoresin of *Picea obovata* were examined.¹⁶⁵⁾

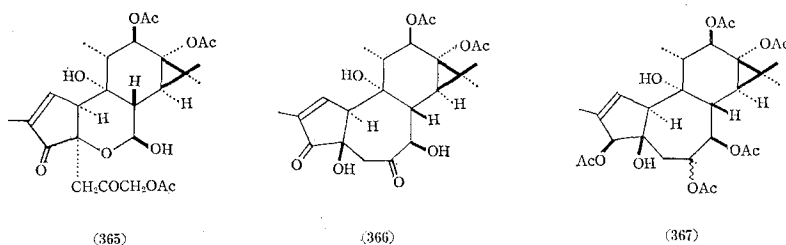
Mass spectra of some diterpene lactones, that is, 12-norambrienolide (356) and its 2 β -hydroxy-, 8-epi-, 2 β -hydroxy-8-epi-, 2-oxo-8-epi-, and 2-oxo-derivatives, and ambrienolide (357) and its 8-epimer, were investigated. Consequently, the following facts were clarified. The molecular ions of some diterpenoid *trans*- γ - and δ -lactones lose the elements of carbon dioxide. The corresponding *cis*-lactones do not undergo fission in this manner. A mechanism for this stereoselective fragmentation was proposed.¹⁶⁶⁾

Several reports on the chemistry of phorbols were published. Oxidation of phorbol pentaacetate (358) with one mole of osmium tetroxide yielded small amounts of triol 359. As the main product, diol 360 was obtained in addition to 361. Oxidation of phorbol triacetate 362 mainly yielded triacetate 363, besides

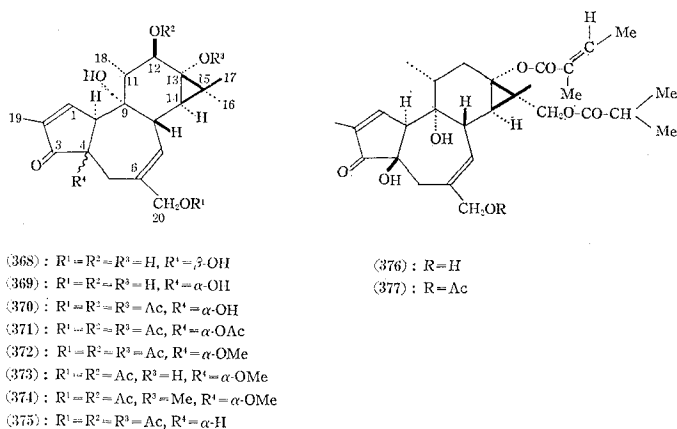
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some diacetate 364. By cleavage of 363 with sodium periodate or lead tetraacetate the expected 6,7-seco compound was obtained as its hemiacetal 365. The corresponding cleavage of 364 yielded 366. By reduction with sodium borohydride and subsequent acetylation, 366 was converted into 367. This compound showed some interesting long range coupling in its NMR spectrum.¹⁶⁷⁾



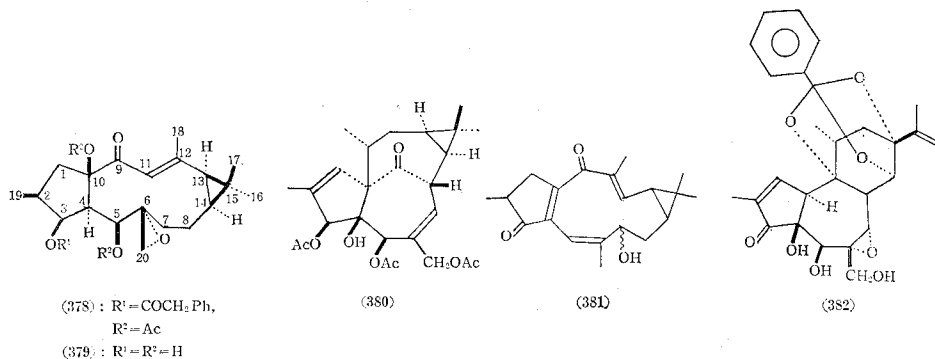
From the mother liquor of preparations of phorbol (368), an isomer 369 (isophorbol) was isolated. This compound was obtained from phorbol by base-catalyzed epimerization. In contrast to phorbol, base-catalyzed acetylation of 369 yielded both 370 and 371. By methylation of 370 with methyl iodide-silver oxide in dimethylformamide three products were obtained : 372, 373 and 374. On reduction with zinc and acetic acid, 370 yielded 375.¹⁶⁸⁾



From latex of *Euphorbia cooperi*, two new irritant and tumor promoting compounds, di-(376) and tri-(377) esters of 16-hydroxy-12-desoxyphorbol were isolated

and characterized.¹⁶⁹⁾

Dilution of the seed oil of *Euphorbia lathyris* with acetone resulted in the separation of a crystalline compound, previously named "euphorbiasteroid." This substance was the diacetate-phenylacetate 378 of a diterpene alcohol 379, for which Hecker *et al.*¹⁷⁰⁾ proposed the name 6, 20-epoxylathyrol. The geometry of the double bond at C-11 had not been known, but recently, an x-ray analysis¹⁷¹⁾ confirmed the structure 378 and elucidated the trans-configuration of the double bond.



A new irritant and cocarcinogenic hexadecanoic acid monoester, $\text{C}_{36}\text{H}_{58}\text{O}_6$, was isolated from the latex of *Euphorbia ingens* and from the seed oil of *E. lathyris*. This substance was subjected to a mild base-catalyzed transesterification to afford biologically inactive resinous parent diterpene alcohol (ingenol), which was converted into a crystalline triacetate. The x-ray analysis of the latter compound confirmed its structure 380.¹⁷²⁾

A new diterpene, the structure (381) of which was closely related to 379, was isolated from a *Bertya* sp. nov., named bertyadionol, and characterized.¹⁷³⁾

Daphnetoxin, the poisonous principle of *Daphne mezereum* and other species of the thymelaeaceous genus *Daphne*, was isolated from methylene chloride extracts of *D. mezereum* bark or commercial "mezeron" bark (*D. mezereum*, *D. laureola*, and *D. gnidium*), and its bisbromoacetate was subjected to an x-ray analysis. Consequently, the structure of daphnetoxin was determined as shown in formula 382.¹⁷⁴⁾

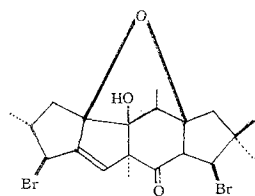
A novel macrocyclic diterpenoid tumor inhibitor, named jatrophone, was isolated from *Jatropha gossypifolia*, and characterized. Dry hydrogen bromide was allowed to react with this substance in glacial acetic acid to yield a dibromo derivative, which was subjected to an x-ray analysis. The structure 383 was confirmed for dibromide and therefore, structure 384 for jatrophone was elucidated. A suspension of 383 with neutral alumina in chloroform was stirred to regenerate 384 in high yield.¹⁷⁵⁾

A brief introduction on some diterpenoids possessing the growth-inhibitory activity for plants was published in Japanese.¹⁷⁶⁾

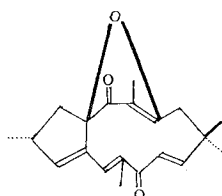
A review on the alkaloids of *Daphniphyllum macropodum* was published in Japanese.¹⁷⁷⁾ The biogenesis suggested that they come from four isoprene units, one acetic acid, and one nitrogen, as shown in formula 385.

A review "biogenetic-type syntheses and reactions of natural products, mainly

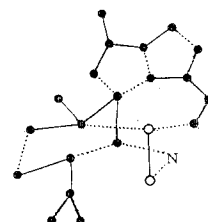
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(383)



(384)



(385): ● isoprene unit
○ acetic acid unit

on terpenoids and simple phenolic compounds" was published in Japanese, in which several syntheses of diterpenoids were described.¹⁷⁸⁾

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